UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

JANSSEN PHARMACEUTICALS, INC., JANSSEN PHARMACEUTICA NV, and JANSSEN RESEARCH & DEVELOPMENT, LLC, Plaintiffs, v. MYLAN LABORATORIES LIMITED, Defendant.	Civil Action No. 2:20-cv-13103-EP-LDW (Consolidated) **HIGHLY CONFIDENTIAL – FILED UNDER SEAL** *Document Electronically Filed*

MYLAN'S OPENING POST-TRIAL BRIEF

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I. INTRODUCTION

Absent this Court's intervention, a lone "missed dose" patent stands to block generic competition of a paliperidone palmitate three-month formulation ("PP3M") for at least another 13 years. This, on top of the 30 years of protection Janssen has enjoyed on paliperidone in some form or another, would create a nearly 50 year monopoly—with the clock still ticking. If Janssen had invented something novel, this serial-patent approach may be warranted. But they did not. Because for PP3M, the active ingredient, drug formulation, methods of use, and even the PP3M initiation dosing regimen were all in the public domain before the filing date of the patent-in-suit.

That is why U.S. Patent No. 10,143,693 ("the '693 patent") thwarts the policy of the Hatch-Waxman Act, which balances enabling low-cost, generic versions of drugs to market while incentivizing pharmaceutical innovation. What speaks volumes to the case at hand, however, is that in the history of the FDA's Orange Book, only two drugs have a lone "missed dose" patent associated with any type of drug exclusivity and they both belong to Janssen. Indeed, this is a case of first impression—where a generic is kept off the market based on a patent directed to what patients should do if they miss a dose of the prior art PP3M formulation, and later desire getting back on treatment. Patient action is what the asserted patent is about—not an inventive formulation or regimen.

So, what should a patient do if they miss their 3-month maintenance dose? Well, it depends on when the patient makes the decision to return for treatment. If it is within four to nine months since their last PP3M injection, Janssen says that patient (who has proven to be non-adherent) should return for three injections over a five-week time period. The irony is that in Janssen's infringement case, no evidence was put forth that the contemplated scenario actually occurs in the real world. That is not surprising—what non-adherent patient is going to magically become adherent for three subsequent injections: two injections one week apart and a third a month later? The flaws are legion.

Fortunately, the law has a way of weeding out such patents. Examining the actual prosecution history of the patent reveals what the patent truly covers, and holds a patentee accountable against taking positions in litigation which are contrary to what it said during prosecution to obtain the patent in the first place. That, too, is before this Court.

Because while the recitation of the aforesaid (and claimed) four to nine month time frame was instrumental in how Janssen obtained the patent, and also now serves as the lynchpin of Janssen's validity defense in this litigation, on the infringement side, Janssen takes a different position and casually calls that very limitation nothing more than an afterthought. To Janssen, a patient missing a dose and voluntarily returning for treatment is simply a clinical descriptor—it is an affliction the patient shows up with prior to being administered any drug—and not

an active step required by the claims. That strains credulity at best, and is hypocritical at worst. Holding Janssen to its prosecution history statements (as the law requires), two actors are required to practice the claims; and because they do not act jointly, there can be no infringement.

Moving on: even if Janssen could somehow get past the preceding hurdle (which it cannot), Janssen would have to separately prove that Mylan had the specific intent to induce others to infringe. There is no such evidence. One need look no further than the indicated use of Mylan's proposed generic PP3M product to glean that the indications themselves have nothing to do with missed doses. If anything, the import of the label is to encourage avoiding missing a dose (and thereby not infringing). And, if the label is to be the end-all be-all for Janssen's infringement theory, then it also bears noting that the vast majority of uses described in Mylan's label, beyond the "Indications and Usage" section, are non-infringing. That is not disputed. And while Mylan's proposed prescribing information includes information related to "missed doses" (as it must under the law) in one isolated section, that very same section [redacted]. A finding of infringement here would be the proverbial tail wagging the dog—a patent claim outside of the FDA approved "Indications and Usage" section for a patient missing a dose that is expressly cautioned against (and lacking any evidence of actual use)—blocking schizophrenic patients from access

to Mylan's lower cost bioequivalent version of the medication. Precedent forecloses this finding.

Validity of the '693 patent fares no better. The reason Janssen could not obtain patent protection for the "Indications and Usage" of PP3M discussed above is because that was disclosed in the prior art JAMA article. This is where the validity case is most interesting: Janssen never disclosed JAMA to the patent office when prosecuting the '693 patent. Without JAMA before the patent examiner, there was no prior art that discussed how a one month paliperidone palmitate formulation ("PP1M") could be used with a PP3M and how dosages of the two formulations could be converted. With JAMA, that, of course, was known.

There was also an abundance of prior art related to PP1M. Janssen had already commercialized a particular PP1M formulation and included (in prescribing information and elsewhere) missed dose information for that formulation. With the exact timing and location of reinitiation loading doses and the maintenance dose disclosed in the prior art, Janssen is left to argue that the middle window of four to nine months was not expressly stated in the prior art. Putting aside that during its infringement case, this four to nine month window means little to Janssen, the case before this court is not one based on anticipation where such a requirement would be necessary. The case here is obviousness. And, with obviousness, the requirement is a showing of a reasonable expectation of success. That is met here, as a POSA identifying the middle window for PP3M

would apply known pharmacokinetic principles to the middle window of PP1M along with routine optimization as directed from other prior art. A person of ordinary skill in the art ("POSA") would be motivated to apply that missed dose information for PP1M to PP3M. And in so doing, the POSA would arrive at the claimed subject matter—no surprises, no extenuated experimentation, no ingenious leaps. Textbook obviousness. *See infra* § III.

There is more. Janssen claimed far more than anything it had in its possession or was enabled in the specification of the patent. If Janssen had claimed the PP1M formulations disclosed in the prior art and incorporated by reference into the specification of the '693 patent, and only the corresponding PP3M formulations, then admittedly, there would be no issue. But Janssen claimed *all* PP1M and *all* PP3M formulations—many of which had never been developed or tested by anyone, let alone Janssen. If a patentee chooses to pursue claims of such broad breadth, then the specification must enable all of those formulations, and must separately show possession of all such formulations. Neither is satisfied here.

II. JANSSEN FAILED TO PROVE INFRINGEMENT

Janssen bears the burden of proving infringement by a preponderance of the evidence. *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1568 (Fed. Cir. 1997). That burden never shifts. *See, e.g., Medtronic, Inc. v. Mirowski Family Ventures LLC*, 571 U.S. 191, 198-99 (2014). And, because the infringement allegations here are based solely on induced infringement pursuant to 35 U.S.C. § 271(b), Janssen

had to "prove [both] (1) direct infringement and (2) 'that [Mylan] possessed specific intent to encourage another's [direct] infringement and not merely that [Mylan] had knowledge of the acts that constitute infringement.'" *Vanda Pharm. Inc. v. West-Ward Pharm. Int'l Ltd.*, 887 F.3d 1117, 1129 (Fed. Cir. 2018) (quoting *DSU Med. Corp. v. JMA Co.*, 471 F.3d 1293, 1306 (Fed. Cir. 2006)). The evidence bore out neither element of induced infringement.

A. No Direct Infringement—Janssen Cannot Show that a Single Entity Would Practice All Steps of the Claim

Direct infringement under an induced infringement theory requires that a single party's activities meet all the limitations as claimed. In other words, to infringe a method claim, "a [single] person must have practiced all steps" of the claim. *Lucent Techs., Inc. v. Gateway, Inc.*, 580 F.3d 1301, 1317 (Fed. Cir. 2019).[1] At trial, no evidence demonstrated that a single "person" practiced all steps of the claim. Rather, the claims at issue clearly require action from two individuals: a patient and a healthcare professional ("HCP"). And those actions are not conducted jointly or solely at the direction of a single actor, the HCP. Instead, (i) a patient must miss a dose contrary to an HCP's direction and by his or her own volition,

[1] There is a limited exception to the requirement that a single actor perform all steps of a claim if "the acts of one are attributable to the other such that a single entity is responsible for the infringement." *Eli Lilly & Co. v. Teva Parenteral Medicines, Inc.,* 845 F.3d 1357, 1364 (Fed. Cir. 2017) (quoting *Akamai Technologies, Inc. v. Limelight Networks*, 797 F.3d 1020, 1022 (Fed. Cir. 2015) ("*Akamai V*"). As detailed *infra*, Janssen failed to allege, much less prove, any type of attribution.

wish to get back on to treatment; and then (ii) an HCP must administer multiple injections to that patient over a course of several weeks. Because such a patient and HCP are not working as a joint enterprise (or one at the direction of the other), an induced infringement theory cannot be maintained.

The dispute between the parties centers on whether the preamble language "wherein said patient had been last administered a PP3M injection 4 to 9 months ago" is a step of the claim. Neither party disagrees that this language requires a patient missing a dose and returning for further treatment within a finite period of time. *See* FOF ¶¶ 268-69. The dispute instead is whether the verbiage in the preamble is an actual step of the claim, as Mylan contends, or simply a clinical descriptor, as Janssen believes.

There is, of course no prohibition to language in a preamble serving as a step of a claim. *Catalina Mktg. Int'l, Inc. v. Coolsavings.com Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002) (quoting *Pitney Bowes, Inc. v. HewlettPackard Co*., 182 F.3d 1298, 1305 (Fed. Cir. 1999) ("a preamble limits the invention if it recites essential structure or steps"). Despite its arguments at trial, Janssen already acknowledged the appropriate analysis that governs the determination of a step in a claim. As Janssen noted, the "law is clear that the **steps of a method claim are actions that must be 'carried out' for infringement to occur**." D.I. 81 at 6 (quoting *Limelight Networks, Inc. v. Akamai Techs., Inc.*, 572 U.S. 915, 921 (2014)) (emphasis added). "Thus, identifying the 'steps' of a method claim simply means identifying what

actions the patent teaches." *Id.* Where those actions appear—including in the preamble—is irrelevant.

a) The Patient Action as Set Forth in the Preamble Must be Carried Out for Infringement to Occur

Focusing on the "action" required by the claim, Claim 5 requires specific "actions," *i.e.*, a patient must miss a dose of PP3M and return for treatment within the recited four-to-nine month period from his or her last PP3M injection. *See* FOF ¶¶ 268-271, 123. Those actions must be "carried out" in order for infringement to occur. And one need look no further than to Janssen's own expert, Dr. Sommi, who's repeated concessions at trial underscore the point. For example, Dr. Sommi testified that infringement would not occur if a patient never missed a dose. FOF ¶ 270. Even if a patient did miss a dose but never returned, then there would be no infringement. *Id.* Dr. Sommi also acknowledged that if a patient missed a dose and returned as little as one day before four months, or as much as one day after nine months, there would be no infringement. FOF ¶ 271. Those concessions further align exactly with the position Janssen took during prosecution in obtaining this patent in the first place.

Because when Janssen's patent was rejected by the patent office and Janssen needed to explain why allowance of its patent was warranted, Janssen pointed to patient action as the distinguishing and novel feature. FOF ¶ 256. In overcoming the rejections of all pending claims as both obvious pursuant to 35 U.S.C. § 103

and failing for nonstatutory obviousness-type double patenting ("OTDP"), Janssen noted:

> The instant claims are solely directed to what **patients** should do if a dose of PP3M is missed and **they** desire getting back on the medication.
>
> [The prior art, Osborne] also does not discuss what to do if a **patient misses** a dose of a long acting injectable medication and **wishes** to get back onto that medication.

DTX-008.0217 and .0216, respectively (emphasis added); FOF ¶¶ 2, 256-57. Whether it be Janssen's expert at trial or Janssen before the patent office, the takeaway is the same: the claims are directed to what patients should do if they miss a dose and desire to get back on medication (*i.e.*, practice a key step of the claim).

To drive the point home, Dr. Sommi was asked a hypothetical where all three administering steps of Claim 5 are carried out, the patient returned for treatment outside of the four to nine month period. FOF ¶ 273. He agreed there would be no infringement in that situation because the patient action of returning in the four to nine month window was not "carried out." *See* FOF ¶¶ 268, 273. This is why the claims must require patient action. If the drug administration steps were the only steps of the claim, as Janssen asserts, then each one of such steps could be "carried out" and yet infringement would still not occur due to the patient's actions.

Dr. Sommi's concession ends the inquiry. And so does common sense. The claims are directed to what a patient should do if a dose is missed.[2] To find otherwise would run afoul of "[t]he public notice function of a patent and its prosecution history [that] requires that the patentee be held to what he declares during the prosecution of his patent." *Spring Window Fashions LP v. Novo Indus., L.P.*, 323 F.3d 989, 995 (Fed. Cir. 2003).

b) A Patient Missing a Dose is Not a "Descriptor of the Clinical Situation"

The preceding discussion helps put Dr. Sommi's other testimony in perspective. To support Janssen's position on infringement, Dr. Sommi argued that the entire preamble is merely "a descriptor of the clinical situation" and "the situation is in patients who have - - that are in need of treatment for psychosis, schizophrenia or bipolar disorder that have been treated with PP3M and they were last administered an injection four to nine months ago." FOF ¶ 279. In other words, "[i]t just helps [him] understand who the patient is that [he's] treating."[3] FOF ¶ 280. That opinion was made—purposefully or not—without the benefit of reviewing the prosecution history, which "is often of critical significance in

[2] This also distinguishes Janssen's reliance on *Orexigen Therapeutics, Inc. v. Actavis Labs. FL, Inc.*, 282 F. Supp. 3d 793, 811-12, 818 (D. Del. 2017). D.I. 81 at 5. There, the Court found that no such admissions were present in the intrinsic record, unlike those that are present in this matter. *Id.* at 812.

[3] While Dr. Sommi testified about "treating" patients, as Dr. Berger testified, "Dr. Sommi is a pharmacist. He doesn't treat patients." FOF ¶ 31.

determining the meaning of the claims." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583-84 (Fed. Cir. 1996). This failure was unexplained at trial. FOF ¶ 33.

Putting aside the litigation decisions that may have motivated that strategy, it is unrebutted that Janssen's sole expert on infringement failed to consider critical evidence that would have direct bearing on any infringement opinion. That speaks volumes. On the one hand, there are Janssen's direct statements to the patent office in 2018 describing the claims as being directed to patient action. On the other hand, there is Janssen's litigation expert in 2022—who himself cannot practice the Asserted Claims[4]—without any insight from the prosecution history, offering the opinion that the preamble is merely a "descriptor." *See Trimed, Inc. v. Arthrex, Inc.*, Case No. 18-cv-666 (MN), 2021 WL 1174532 at *6 (D. Del. Mar. 29, 2021) ("courts must not lose sight of the fact that 'expert reports and testimony [are] generated at the time of and for the purpose of litigation and thus can suffer from bias that is not present in intrinsic evidence." (quoting *Phillips v. AWH Corp.*, 415 F.3d 1303, 1318 (Fed. Cir. 2005) (*en banc*)). It is thus difficult to see how Janssen's burden on infringement has been met.

Putting aside that Dr. Sommi's opinion is incongruent with the patent's intrinsic record, the crux of his opinion further runs afoul of his own testimony. As

[4] Janssen asserts claims 5-7 and 9-14 of the '693 patent (the "Asserted Claims").

noted above, Dr. Sommi conceded that it is "true that a patient has to miss a dose of PP3M and return for treatment on at least three occasions" in order for the claim to be infringed. FOF ¶ 269. How can that activity be a mere "clinical descriptor?" A "clinical descriptor" describes the affliction a patient may have. For example, in a patient having schizophrenia, "schizophrenia" would be the "clinical descriptor." Or, in another common refrain from trial, in a patient afflicted with cancer, having "cancer" would be the "clinical descriptor." Contrast that with what is being proffered here: Janssen is disguising the patient actions of missing a dose and returning for treatment as passive. But they are not. The language of the preamble relates directly to patient adherence. It is the patient that chooses to miss a dose. It is also the patient that chooses to return for treatment. Those are active steps, required by the claim, that must be "carried out."

Of course, none of this was lost on Dr. Sommi at trial. As he acknowledged, the '693 patent is about adherence. FOF ¶ 117. Adherence is a term well-known in the art to refer to "the extent to which a patient's behavior corresponds with the advice given by their providers." FOF ¶ 117; DTX-211.0001. Likewise, a patient's nonadherence is a choice, or a conscious decision, not to comply with his or her HCP's advice. FOF ¶ 118. This important fact is one that distinguishes this patent from steps of method of treatment claims having multiple actors working together (either one at the direction of the other or as a joint enterprise). *Eli Lilly*, 845 F.3d at 1364.

Eli Lilly actually demonstrates Mylan's point. There, the claims required that folic acid be administered by a patient prior to the administration of pemetrexed by a physician. 845 F.3d at 1364. The court found that those were two distinct activities conducted by two different actors and, thus, required that, in order to show infringement, the plaintiff needed proof that either that one entity "directs or controls the others' performance" or that the entities formed a "joint enterprise." *Eli Lilly*, 845 F.3d at 1364 (noting that, since Eli Lilly did not pursue a joint enterprise theory, the question relied on whether physicians direct or control their patients' actions). Infringement was found in *Eli Lilly* because the plaintiff introduced substantial evidence to meet the two prong test to establish the principles of attribution[5] as an exception to divided infringement. *Id.* at 1366, 1367.

The Asserted Claims here, like those in *Eli Lilly*, require the action of two distinct actors. But unlike *Eli Lilly*, Janssen failed to introduce evidence of direction or control. That is not surprising. No HCP would ever instruct a patient to miss a dose. FOF ¶ 289. Rather, HCPs direct patients to avoid missing a dose and only if a patient goes against that directive from the HCP will the preamble of Claim 5 be satisfied. *See Eli Lilly*, 845 F.3d at 1367 (emphasizing that the

[5] The principles of attribution apply in "directing or controlling others' performance in circumstances in which an actor: (1) '*conditions* participation in an activity or receipt of a benefit' upon others' performance of one or more steps of a patented method, and (2) '*establishes the manner or timing* of that performance.'" *Eli Lilly*, 845 F.3d at 1365 (quoting *Akamai V,* 797 F.3d at 1023) (emphasis in original).

"Physician Prescription Information, instructs physicians not only to tell patients to take folic acid orally" (a required step) but also was "accompanied with warnings about the consequences of non-compliance" with the claimed step). So unlike *Eli Lilly*, the patient's acts are not attributable to the HCP such that a single entity is responsible for any purported infringement.

Perhaps this is why Janssen attempted to conflate the claims at issue here with run-of-the-mill method-of-treatment claims, including its own '906 patent that covers the initiation of treatment onto PP1M. *See* FOF ¶¶ 255-56. Nowhere in the '906 patent, though, are there steps taken by one actor in contravention of directives from a second actor. The opposite is true. The steps of the '906 patent would be practiced by, or at the direction/control of, an HCP. *See* FOF ¶¶ 255-56. Following *Eli Lilly*, the "factual circumstances [of the '906 patent would be] sufficiently analogous . . . to support a finding of direct infringement by [HCPs]." *Eli Lilly*, 845 F.3d at 1365. That is in no way the situation required by the '693 patent where a patient must miss a dose and return to resume dosage within a finite time.

But the '906 patent—which is directed to an initiation of treatment—can be distinguished from the '693 patent even more easily. As noted above, in order to overcome an OTDP rejection, Janssen obtained the '693 patent by telling the patent office that it was nothing like the '906 patent because the application that became the '693 patent was solely directed to the patient taking the steps of missing a dose and actively desiring to get back on the medication. FOF ¶ 258; DTX-008.0217.

To now find that the steps of the '693 patent are no different in nature from the steps of the '906 patent (considering HCP administration steps, alone) would run afoul of Federal Circuit precedent. *Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1578 (Fed. Cir. 1995) ("A patentee may not proffer an interpretation for the purposes of litigation that would alter the indisputable public record consisting of the claims, the specification, and the prosecution history, and treat the claims as a 'nose of wax.'").

Far from supporting the infringement charge, the '906 patent actually illustrates that Janssen was more than familiar with how to draft method-of-treatment claims where the preamble served merely as "a description of who is going to be treated with that medication." FOF ¶¶ 254-56. But Janssen chose not to take that approach with the Asserted Claims here because, if not for calling out the requirement of patient action to the patent examiner, the patent would never have been allowed. *Chef Am., Inc. v. Lamb-Weston, Inc.,* 358 F.3d 1371, 1374 (Fed. Cir. 2004) (Claims must be construed as written, "not as the patentees wish they had written [them].").

The only question remaining is whether a patient could self-administer PP3M because, if so, the patient would be the sole actor and there would be no

divided infringement. This position is what Janssen originally alleged in this case.[6] And Dr. Sommi made the same allegation before modifying it at trial.[7] But the record is clear. PP3M cannot be self-administered; a second actor (an HCP) is required. FOF ¶ 204. Application of the legal requirements of *Eli Lilly* to the evidentiary record of this case thus clearly mandates a finding of non-infringement.

c) The Specification Supports That the Contested Language of the Preamble is a Step of the Claim

The trial record and claim language is consistent with the patent specification. The '693 specification is replete with references teaching the *action* of the patient missing—or having missed—a dose of PP3M. FOF ¶ 240; DTX-001.0001 (Title and Abstract). There, the specification is no different from the prosecution history and, like the prosecution history, must be considered in understanding the meaning of the claims. "[Courts] cannot look at the ordinary meaning of [a] term in a vacuum but must consider the context of the written description and the prosecution history." *E.I. du Pont De Nemours & Co. v. Unifrax I LLC*, 921 F.3d 1060, 1068 (Fed. Cir. 2019) (internal quotations and citations omitted).

The Abstract could not be clearer in describing the scope of the patent: "[W]herein said patient is being treated with the 3-month formulation of

[6] *See* FOF ¶¶ 36, 46; D.I. 72 at 8.
[7] *See* FOF ¶ 36.

paliperidone palmitate and the patient fails to take the next scheduled dose." DTX-001.0001. Likewise, in describing the embodiment of Claim 5, Janssen stated: "Wherein said patient misses for a period of between about four months and nine months." FOF ¶ 276. "[T]he specification is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Phillips*, 415 F.3d at (quoting *Vitronics Corp. v. Conceptronic, Inc*., 90 F.3d 1576, 1582 (Fed. Cir. 1996)).

Janssen has never explained away its statements in either the prosecution history or the resulting specification. Instead, Janssen made two arguments: (1) Mylan was purportedly re-writing the claims; and (2) the past tense in the preamble prevents the contested language from being a step of the claim. Neither argument has merit.

The plain language of the claims requires certain actions, some from HCPs and others from patients. FOF ¶ 268. What Janssen characterizes as "re-writing" is no more than reading the plain language of the claims as a POSA[8] would. FOF ¶ 264. During Dr. Sommi's cross-examination, Dr. Sommi conceded that each of the purported "re-writes" in the claims is actually required for infringement to occur. FOF ¶ 268. One is not re-writing a claim when the actions at issue are necessary for infringement to occur. That is simply what the claims require as

[8] The parties have agreed to a definition of a POSA as set forth in the final pretrial order (D.I. 99 at SOF ¶ 49) and further presented at trial. *See* FOF ¶ 262.

supported by the specification and file history. *See* FOF ¶ 277 (citing Tr. 194:4-7 (Berger) ("[T]he file history tells what the patent is all about, how we got here, what this patent is intended to do.")); *Vitronics*, 90 F.3d at 1583 (Where, as here, "the public record unambiguously describes the scope of the patented invention, reliance on extrinsic evidence is improper.").

On verb tense, the specification itself undermines Janssen's position and exemplifies how tortured the analysis must be to support a finding of infringement. For example, the specification uses past and present tense interchangeably when describing the same actions: a patient missing or having missed a dose of PP3M and choosing to return for treatment. FOF ¶ 244. The specification at times even refers to the "administering" steps in the past tense. *Id*. at ¶ 245. When a POSA looks to the specification to understand what actions it teaches, it is not the tense that is determinative; rather, it is whether an action must be "carried out" for infringement to occur. The intrinsic record here is clear: for infringement to occur a patient must miss a dose and choose to return for treatment between four to nine months from their previous PP3M injection. *See* FOF ¶¶ 268-69.

B. No Specific Intent

Distinct from the arguments above, Janssen separately failed to establish that Mylan has the requisite intent to induce infringement. Here again, Janssen's infringement allegations rely solely on the text of Mylan's proposed label. FOF ¶ 291. But simply pointing to the similarities between Mylan's proposed prescribing

information and that of Trinza® is not sufficient to meet Janssen's burden. *HZNP Medicines LLC v. Actavis Lab'ys UT, Inc.,* 940 F.3d 680, 701–02 (Fed. Cir. 2019) (upholding summary judgment of noninfringement even when it was "undisputed that Actavis's label is substantially similar to Horizon's; the primary difference between the two labels is that Horizon's label refers to [the brand name] instead of the [generic name].").

That makes sense. While "the proposed label *may* provide evidence of [the ANDA applicant's] affirmative intent to induce infringement," the law requires more because "[t]he label *must* encourage, recommend, or promote infringement." *Vanda Pharms. Inc.*, 887 F.3d at 1129 (Fed. Cir. 2018) (emphasis added) (internal citations and quotations omitted). If all that was required to prove infringement was showing the "sameness" of proposed product information from an ANDA filer to that of a Reference Listed Drug (like Trinza®), then infringement would lie in every ANDA case since the Hatch-Waxman Act requires that "sameness." FOF ¶ 227. But that is not the law. Rather, Janssen must prove that Mylan's proposed product information encourages, recommends, or promotes infringement.

The true focus is on what the actual "Indications and Usage" section of the label instructs because that is what defines the intended use of the drug itself. Thus, infringement can be found where following the "Indications and Usage" results in direct infringement. *See Sanofi v. Watson Labs. Inc.*, 875 F.3d 636 (Fed. Cir. 2017). In *Sanofi*, the Federal Circuit focused on the "Indications and Usage" including the

other portions of the label, as well as "Clinical Studies" which were incorporated therein. *Id.* at 642-43; *id.* at 645 (focusing on those for whom the drug is "indicated" and the "only FDA-approved use"); *id.* at 646 (quoting testimony that "it is important for the [POSA] to look at the label's indication section to see if a drug 'is indicated for administration to patients of certain characteristics with a certain intent").

But, here, the "Indications and Usage" section is indisputably non-infringing. And "[a]n item's inclusion in the Indications and Usage section cannot be brushed aside; to place it there is a critical regulatory decision." *BTG Int'l Ltd. v. Amneal Pharms. LLC*, 352 F. Supp. 3d 352, 392 (D.N.J. 2018); *see Bayer Schering Pharma AG v. Lupin Ltd.,* 676 F.3d 1316, 1321 (Fed. Cir. 2012) (discussing the substantive importance of the "Indications and Usage" portion of a product label). Here, that section recites in relevant part [redacted] FOF ¶ 296; DTX-137.0001. That is the usage that is being encouraged. And the sections of the proposed prescribing information that are incorporated by reference into the "Indications and Usage" all relate to non-infringing uses as well. FOF ¶ 296. The inquiry should end there.

1. The Vast Majority of Mylan's Proposed Prescribing Information Uses Are Non-Infringing

Even if one were to ignore the indications of Mylan's proposed PP3M, the vast majority of other uses pursuant to Mylan's proposed prescribing information would be non-infringing. For example, if one were to follow the information in *any* section aside from Section 2.3 in the label, there would be no infringing use. *See* FOF ¶¶ 300-01. That is true for the entirety of the label, even the main section directed to "Dosage and Administration" which includes only non-infringing uses. *See* FOF ¶¶ 296-97. Indeed, nearly all of the label is for non-infringing uses. By way of example and as explained at trial, if one were to follow Sections 2.1, 2.2, 2.6, and/or 2.7, to name a few, one would never infringe the Asserted Claims.

For that matter, even if one were to focus solely on Section 2.3 of the label—the only section that Janssen points to in support of their infringement contention—most of that section relates to non-infringing uses. *See* FOF ¶¶ 301, 270-71 (Dr. Sommi describing other windows in Section 2.3 that are non-infringing). As mentioned *supra*, Janssen does not contest that the vast majority of patients on PP3M are adherent or fall within another portion of Section 2.3. Rather, it contends only "that, when such need arises, Mylan's instruction will lead to an infringing use." *See* FOF ¶ 210; *HZNP*, 940 F.3d at 701.

As noted during the cross-examination of Dr. Berger, the Asserted Claims operate in an "if/then" manner. FOF ¶ 210. The label is "saying don't miss doses,

but if you do miss doses, [redacted][9] *See* FOF ¶¶ 208, 210. But "permission does not amount to encouragement because those items are just [] examples of what a patient might wish to [do after treatment, if anything]." *HZNP*, 940 F.3d at 702. Because portions of prescribing information that operate in an "if/then" manner can "not encourage infringement, particularly where the label does not require [missing a dose]," there cannot be a finding of specific intent. *Id.*; *see id.* ("*if* the user wants to cover the treated area with clothing or apply another substance over it, *then* the patient should wait until the area is dry. This does not encourage infringement[.]") (emphasis in original).

2. Infringement Is Not Inevitable, Nor Is Inevitability the Standard for Infringement

Against the foregoing, the axiom pushed by Janssen was that Mylan's proposed information would "inevitably" lead to some, unquantified infringement. FOF ¶ 281. Essentially, as long as the label "would inevitably lead somebody, a healthcare professional, to infringe, [] that would establish the inducement." *Id.* That is not the law. "The mere existence of direct infringement by physicians, while necessary to find liability for induced infringement, is not sufficient for

[9] This again is evidence of the inconsistencies of Janssen's position, including those of its own expert, when it comes to whom the claims are directed. Here, Janssen's counsel, while questioning Dr. Berger on Mylan's proposed prescribing information, insists that this portion of the label is telling *patients* [redacted] *but*, if *they* do, [redacted]. FOF ¶ 208; *but see* FOF ¶ 277 (Tr. 86:20-22 (Sommi)).

inducement." *Eli Lilly & Co.*, 845 F.3d at 1368 (quoting *Takeda Pharm. USA, Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 631 (Fed Cir. 2015)).

Even the testimony at trial elicited from Janssen's expert did not move the needle. First, Dr. Sommi was asked: "Q: Is it inevitable that health care professionals will infringe Claim 5 of the '693 patent *if they follow* the missed dose instructions in Mylan's label?" FOF ¶ 281 (quoting Tr. 99:22-25 (Sommi)) (emphasis added). He responded in the affirmative. But that is not the proper standard. "[I]n the ANDA context, it is well-established that 'mere knowledge of possible infringement by others does not amount to inducement; specific intent and action to induce infringement must be proven.'" *Takeda*, 785 F.3d at 631 (quoting *Warner-Lambert*, 316 F.3d at 1364). The label or other evidence[10] still must encourage, recommend, or promote an infringing use.

There was a follow-up: "Q: Do you have any doubt about whether Mylan's proposed label instructions will inevitably induce infringement of the asserted '693 patent claims?" FOF ¶ 281. Dr. Sommi answered in the negative. No proof or explanation—just a speculative "no." *Id*. But "speculation or even proof that some, or even many, doctors would prescribe [the drug in an infringing manner] is hardly evidence of inevitability." *Takeda*, 785 F.3d at 633. The only other discussion as

[10] Dr. Sommi did not review any materials outside of Mylan's proposed prescribing information, such as any internal Mylan materials or even Janssen materials for that matter. FOF ¶¶ 291-92.

to what was "inevitable" was about the possibility of patients missing doses. FOF ¶ 119 (quoting Tr. 65:16-17 (Sommi) ("Do we wait until [patients] show us that they're going to do the inevitable and then it's missed doses?")). That is not the claim though; Claim 5 is not directed solely to a patient missing a dose. *See* FOF ¶ 268. Unsupported conjecture is not tantamount to inevitability.

That was highlighted by Mylan's expert, Dr. Berger, at trial. Dr. Berger testified that the information included in the Trinza® label would not be followed by a practicing physician. *See* FOF ¶¶ 309-12. The reason happens to be the most logical: the only way "Missed Dose" information comes into play is, naturally, if a patient misses a dose. If that occurs, and the patient returns for treatment on his or her own volition, the HCP is then working with a patient that has shown to be non-adherent and the "Missed Dose" information calls for two injections of PP1M a week apart followed by a PP3M injection a month later. *See* FOF ¶ 314; Tr. 126:2-8 (Sommi) (impeachment); Tr. 203:13 (Berger) ("Both patients have proven themselves to be nonadherent."). Dr. Berger explained that attempting to get a non-adherent patient to switch gears and be adherent is not how an HCP would operate in the real world. *See* FOF ¶¶ 212, 312. Instead, an HCP, like Dr. Berger, would potentially dose adjust and/or administer a single PP3M injection to provide the patient with the longest potential dose and not ask the non-adherent patient to come back repeatedly in a month's time for multiple injections. *See* FOF ¶ 314. As a practicing physician treating tens of thousands of patients, neither Dr. Berger nor

any of his residents have ever been able to follow the information provided in the Trinza® label with respect to a patient who has missed a dose and returns for treatment four to nine months after his/her last PP3M injection. *See* FOF ¶ 282. And nothing at trial—let alone on cross-examination—undermined Dr. Berger's testimony in this regard.

Against Dr. Berger's uncontroverted testimony, it is telling that Janssen chose to forego any testimony from a prescribing physician who had or would follow the claimed missed-dose regimen. Instead, Janssen sought testimony from a healthcare professional who does not have prescribing rights for the drug at issue: Dr. Sommi, a pharmacist.[11] For his part, Dr. Sommi testified that his clinical work, outside of clinical trials,[12] involves "giv[ing] some verbal recommendations to the nurse practitioner and the psychiatrist about what could be done in terms of managing, what [he] thinks is going on with that patient from a medication point of view, and then [he] prepare[s] a written report . . . that goes into the patient's record." FOF ¶ 282 (quoting Tr. 49:22-50:2 (Sommi)).

[11] While Dr. Kohler testified for Janssen on secondary considerations, Janssen did not ask Dr. Kohler to testify on infringement and objected to any Mylan questioning on that topic. FOF ¶ 62; *see also* FOF ¶ 64.

[12] And as Dr. Sommi testified, in the case of clinical trials, these are patients who are different from those in the real-world because in clinical trials they are "all patients who were actively engaged in wanting to get injections." FOF ¶ 282; Tr. 648:11-13 (Sommi).

That testimony speaks volumes to what knowledge—or lack thereof—Dr. Sommi has regarding physician practice and the treatment of patients. It establishes that Dr. Sommi does not have any personal knowledge about whether or not any patient has actually been treated in accordance with Claim 5 or whether such treatment would be likely to occur. *See* FOF ¶ 286. Nor does he have any idea of what percentage of patients miss their doses and return for treatment exactly between four to nine months after their last dose of PP3M, let alone return multiple times thereafter as required by Claim 5. *See* FOF ¶ 286. Because as he testified, it is the "physicians [who] have access to the medical record" not the pharmacists. *See* FOF ¶ 286. Dr. Sommi summed it up best when he unequivocally admitted that he did not show any evidence of direct infringement of the Asserted Claims. *See* FOF ¶ 281; Tr. 132:4-6 (Sommi) ("Q: . . . You have not shown any evidence, correct? A: Correct.")[13]; *see Genentech, Inc. v. Sandoz Inc.*, 55 F.4th 1368, 1380 (Fed. Cir. 2022).

[13] Of course, even in the absence of personal knowledge, Dr. Sommi could have relied on anonymized patient data or surveys of physicians/physician practice. He chose not to. This omission was especially glaring because Janssen introduced an article authored by a Janssen employee who had access to data that tracked individual patients as they were administered PP1M and PP3M over time. FOF ¶ 7; DTX-176. While that information was likely available to Dr. Sommi—as it was to Janssen's other experts—he did not rely on it. Accordingly, the only evidence (including that relating to the lack of direct infringement) of a practicing physician, presented at trial was from Mylan's expert, Dr. Berger.

If anything, Dr. Sommi's testimony supports a finding of non-infringement. He testified that, instead of waiting four to nine months, as soon as a patient does not show up for an appointment a doctor would encourage the patient to come get his/her shot as soon as possible—going so far as to say that if he knew a patient missed a dose, he might go out and find them. *See* FOF ¶ 304. No HCP will ever instruct a patient to only return four to nine months from his/her last injection. *See* FOF ¶ 289. But that is the absurd result needed for infringement to take place.

Finally, and to bring the discussion back to the label itself and how it rounds this notion of "inevitability" that Janssen advances, if there is any inevitable result, it is that the generic version of PP3M that Mylan would market would "inevitably" be prescribed substantially for non-infringing uses. In other words, as this Court previously explained, if Janssen "must engage in [a] 'scholarly scavenger hunt' through the label to identify statements that may potentially, but not inevitably, impact a prescribing physician's actions" the inducement claim should be rejected. *BTG Int'l*, 352 F. Supp. 3d at 393 (crediting Judge Sheridan's analysis in *United Therapeutics Corp. v. Sandoz, Inc.*, Case No. 12-cv-1617, 2014 WL 4259153, at *18 (D.N.J. Aug. 29, 2014)). When a product has such substantial non-infringing uses as those discussed above, "intent to induce infringement cannot be inferred even [if the defendant] has actual knowledge that some users of its product may be infringing the patent." *HZNP*, 940 F.3d at 702 (Fed. Cir. 2019) (*quoting Warner-*

Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1365 (Fed. Cir. 2003)). The infringement charge must fail.

3. Mylan Discourages Infringement

Mylan's proposed prescribing information, [redacted] includes two explicit warnings that [redacted] *See* FOF ¶ 5; DTX-137 at 1, 6. "[T]here is a rather significant difference between a warning and an instruction." *See Takeda Pharms. USA, Inc. v. W.-Ward Pharm. Corp.*, 72 F. Supp. 3d 539, 547 (D. Del. 2014), *aff'd* (Jan. 9, 2015), *aff'd in part, appeal dismissed in part sub nom. Takeda Pharms. U.S.A., Inc. v. W.-Ward Pharm. Corp.*, 785 F.3d 625 (Fed. Cir. 2015) (finding no inducement where the label described infringing use as something that "should be avoided"). It cannot be that Mylan simultaneously instructs physicians and patients to [redacted] while at the same time encourages them to miss a dose and reinitiate treatment in a particular manner.

That is why both parties' experts agreed that *if* a patient misses a dose, it would be going "against Mylan's proposed prescribing information." *See* FOF ¶¶ 306, 308. Anyone following Mylan's proposed prescribing information would "instruct [patients] to not miss doses and show up for [their] appointments and do everything [physicians] want you to do." *See* FOF ¶ 304. It defies logic to suggest that Mylan's proposed prescribing information will encourage HCPs to go against the standard of care and best practices in order to use PP3M in an infringing

manner. Janssen's corporate witness even confirmed that Janssen, as a pharmaceutical company, does not encourage HCPs and/or patients to miss doses. *See* FOF ¶ 292. And Janssen "[c]ertainly [] would want patients to stay on treatment because if they stay on treatment, they get the benefit of the drug." *See* FOF ¶ 292. This aligns with all experts' testimony because, as Dr. Sommi stated, one of the single most important things HCPs treating patients with schizophrenia can do is try to get them to stay on their medication. *See* FOF ¶ 306.

Accordingly, Janssen has failed to meet its burden to establish infringement and, thus, the Court should find that Mylan does not induce infringement of the '693 patent.

III. THE ASSERTED CLAIMS ARE INVALID AS OBVIOUS PURSUANT TO 35 U.S.C. § 103

Mylan satisfied its burden of proving obviousness by a clear and convincing evidence standard. That burden does not apply to the ultimate legal conclusion of obviousness itself; rather, it applies to the disputed facts underlying the conclusion of obviousness. *Newell Cos., Inc. v. Kenney Mfg. Co.*, 864 F.2d 757, 767 (Fed. Cir. 1988).

In an obviousness analysis, the Court is charged with assessing: (1) the scope and content of the prior art, (2) the level of ordinary skill in the art (not disputed here), (3) the differences between the claimed invention and the prior art, and (4) the so-called "secondary considerations." *Graham v. John Deere Co.*, 383 U.S. 1

(1966). That obviousness analysis differs significantly from anticipation pursuant to 35 U.S.C. § 102 (not at issue in this case) because "[o]bviousness can be proven by combining existing prior art references, while anticipation requires all elements of a claim to be disclosed within a single reference." *Cohesive Techs., Inc. v. Waters Corp.,* 543 F.3d 1351, 1364 (Fed. Cir. 2008).

Based on the testimony from Janssen's experts, it is evident that Janssen wants to conflate the standard for a showing of obviousness with that of anticipation. But that is improper. *In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986) ("Non-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references.") (citing *In re Keller*, 642 F.2d 413, 425 (CCPA 1981)). In an obviousness analysis the Court must assess "the prior arts' teaching as a whole in light of the creativity and common sense of a person of ordinary skill." *Duramed Pharms., Inc. v. Watson Labs., Inc.*, 413 F. App'x 289, 294 (Fed. Cir. 2011).

When applying the appropriate legal framework (*i.e.*, obviousness, not anticipation), this case is straightforward. Paliperidone palmitate was known in the prior art, including its pharmacokinetic properties in an FDA-approved PP1M formulation, and that it could be used to treat schizophrenia. And, like with all chronic illnesses, it was known that patients may miss a scheduled dose. Most relevant to the missed dosing regimen claimed here, the prior art specifically taught what to do with a patient who misses a dose and returns after a moderate period of

time (where some drug remains in the body but is insufficient to get back into steady-state): administer two PP1M injections in the deltoid, a week apart from each other. It was further known that, a month after that, one should administer to the patient his or her normal maintenance dose. This prior-art teaching of how to handle such patients was not speculative; it was backed by clinical data and the specific missed dosing regimen was on the FDA-approved Invega Sustenna® label.

It takes little "creativity and common sense" for a POSA to take those teachings and apply them in the exact same way to the same type of patient missing a PP3M dose (the JAMA article referenced above teaches a safe and effective PP3M formulation (FOF § XI.D (DTX-026))). Mylan's expert Dr. Forrest explained the obvious—if a patient missed a PP3M dose for a moderate amount of time, a POSA would get the patient back into steady state by doing the same thing (two PP1M injections one week apart in the deltoid)—and then return to maintenance dosing one month later. A POSA would have no qualms about using a PP1M formulation with patients on a PP3M formulation because JAMA provided that initiation onto PP3M (which is getting into steady state) should be done using PP1M and even provided the specific conversions between equivalent PP3M and PP1M dosages. FOF ¶¶ 365-366. As Dr. Forrest explained, a POSA would naturally expect that, for reinitiation back onto PP3M after a patient misses a dose, using PP1M to get the patient back to steady state and then progressing to the PP3M dose to maintain that steady state would make sense. FOF ¶ 369.

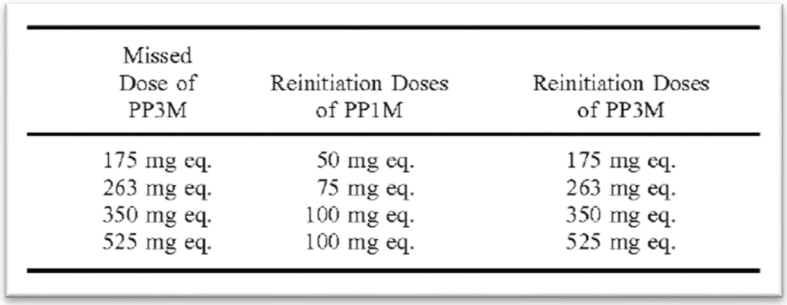
Applying the teachings of the prior art to delineate PP3M missed-dose information results in exactly what Janssen says are the only steps necessary to perform the claimed invention. Confirming that the prior art methodology also worked for PP3M patients in the same situation might have required work. But the patent laws do not reward work with a monopoly; they only reward innovation. *KSR Int'l v. Teleflex Inc.*, 550 U.S. 398, 415-16 (2007) ("need for caution in granting a patent based on the combination of elements found in the prior art" as doing so would "withdraw[] what already is known in the field of its monopoly and diminish[] the resources available to skillful [wo]men"). There is no spark of genius here. There is nothing unexpected. To the contrary, the Asserted Claims are no more than an expected approach to an expected problem. *Id*. at 421.

All that would remain is determining the timeframe window when such an expected approach would make sense. The parties dispute whether the exact range of four to nine months since the last administration would be taught by the prior art. But there was agreement by the experts that certain months in that range—*i.e.*, a patient returning between six months and nine months would fall into the middle window. *See* FOF ¶ 410. Mylan submits that the agreement between the parties that six to nine months would fall within the middle window based on the prior art is sufficient for a finding of invalidity. But, even if an exact window of four to nine months was required to establish obviousness of when a patient chooses to return after missing a dose of a PP3M formulation, Dr. Forrest explained how basic

pharmacokinetic principles could be used and would lead a POSA to that exact range through routine optimization. FOF § XII.A.4.

This is Mylan's obviousness argument. It is straightforward and requires no more than "use of [] known technique[s] to improve similar methods or products in the same way." M.P.E.P. § 2143; FOF ¶ 41. But one need not take Mylan's word for it. The prior art bears it out. The below chart provides where within this brief the teachings of the prior art lead a POSA to what Janssen claimed in Claim 5.

Prior Art Teachings	**Claim 5 Element**
Section III.B.1	A dosing regimen for administering an injectable paliperidone palmitate depot to a patient in need of treatment for psychosis, schizophrenia or bipolar disorder that has been treated with PP3M
Sections III.B.5, III.B.6	Wherein said patient had been last administered a PP3M injection 4 to 9 months ago and the next scheduled maintenance dose of PP3M should be administered to said patient, comprising:
Sections III.B.4 III.B.6	Administering intramuscularly in the deltoid muscle of said patient a first reinitiation loading dose of PP1M
Sections III.B.4 III.B.6	Administering intramuscularly in the deltoid muscle of said patient a second reinitiation loading dose of PP1M on about the 4th day to about the 12th day after administering of said first reinitiation loading dose; and
Sections III.B.4 III.B.6	Administering intramuscularly in the deltoid or gluteal muscle of said patient a reinitiation dose of PP3M on about the 23rd day to about the 37th day after administering the second reinitiation loading dose of PP1M wherein said first and second reinitiation loading doses are selected from the table below based on the amount of the missed dose

Section III.B.6	

Missed Dose of PP3M	Reinitiation Doses of PP1M	Reinitiation Doses of PP3M
175 mg eq.	50 mg eq.	175 mg eq.
263 mg eq.	75 mg eq.	263 mg eq.
350 mg eq.	100 mg eq.	350 mg eq.
525 mg eq.	100 mg eq.	525 mg eq.

A. The Scope and Content of the Prior Art

The scope and content of the prior art is relevant to obviousness as well as the enablement and written description requirements pursuant to 35 U.S.C. § 112 (discussed *infra* §§ V.A-B). And, as both sides agree, the teachings of the prior art should be viewed through the lens of a POSA. *KSR*, 550 U.S. at 420. While different elements of the prior art may bear more relevance to one invalidity inquiry over another, the prior art's teaching should be applied consistently across all three. That is exactly what Mylan did at trial. Mylan presented the testimony of Dr. Forrest who consistently applied the prior art teachings to each basis for invalidity. Janssen, on the other hand, presented multiple experts who were isolated, did not review all of the prior art, and/or provided flatly inconsistent positions on the teachings of the prior art. *See, e.g.*, FOF ¶¶ 63-64 (Kohler), 33-35 (Sommi); 51-53 (Little); 58-59 (Gobburu).

1. Background Knowledge on Schizophrenia

There is no dispute that schizophrenia[14] is a debilitating, chronic mental affliction that impacts hundreds of thousands of Americans. *See* FOF ¶¶ 102, 105. There is still no cure; rather there are only medical treatments to manage the symptoms. *See* FOF ¶ 106-07. One of the main goals of treatment is relapse prevention. *See* FOF ¶ 107.

As discussed at trial, the drug compounds most pertinent to the issues presented here are risperidone, paliperidone, and paliperidone palmitate. FOF ¶¶ 182-84. Each of these were used in drug formulations for the treatment of schizophrenia as of the priority date, beginning with risperidone (1993), Risperdal Consta (2003), paliperidone (2006), and then paliperidone palmitate (2009). FOF ¶ 181. And each of these drugs are interrelated. Paliperidone is the major active metabolite of risperidone and paliperidone palmitate is a paliperidone ester, which is the stable form used in paliperidone LAIs. FOF ¶ 181. The fact that these compounds are interrelated is relevant to invalidity because a POSA could expect that "compounds with common properties are likely to share other related properties as well." *Valeant Pharms. Int'l, Inc. v. Mylan Pharms. Inc.*, 955 F.3d 25, 32 (Fed. Cir. 2020).

[14] The parties agree that schizophrenia is a form of "psychosis", as stated in claim 5, and so schizophrenia falls within the scope of all of the Asserted Claims. In fact, multiple experts testified that psychosis is merely a bucket term for patients which "include[s] schizophrenia." FOF ¶¶ 103, 417.

A specific PP1M formulation was known and commercialized by Janssen at least as early as 2009 under the brand name of Invega Sustenna®. FOF ¶ 328. Invega Sustenna® is a paliperidone palmitate injectable suspension indicated for the treatment of schizophrenia. FOF ¶ 184. The prescribing information for Invega Sustenna® ("the Sustenna Label") provided that it should be administered intramuscularly once monthly and included information about "missed doses" that a physician could consider when a patient missed a dose. FOF ¶¶ 328, 344. Not only was this information disclosed by Janssen in the Sustenna Label, but Janssen saturated the prior art with knowledge regarding paliperidone and its pharmacokinetic properties, as discussed in more detail below.

2. Background Knowledge on Pharmacokinetics and "LAI" Formulations

Patient compliance has long been an issue in the treatment of all chronic illnesses. FOF ¶ 119. One way providers have attempted to combat this issue is to develop depot drugs, which allow for drugs to be given at less frequent dosing intervals, including monthly, four-month, and 6-month intervals. FOF ¶¶ 120-21. That development is no different in the field of antipsychotic medications. FOF ¶¶ 111-14. There, formulations were developed utilizing established concepts, including preexisting "depot formulations" and known pharmacokinetic concepts.

Pharmacokinetics ("PK") refers to the concentration of a given drug in the body, which is usually measured in the bloodstream. FOF ¶¶ 125-126. In

developing a drug likely to be effective in the body for a longer period of time—such as a month or more—it is desirable to establish a way for the drug to be present in the bloodstream in an effective concentration for that entire period. FOF ¶¶ 158, 160. The concentration of a drug in the body is determined by its absorption (how it enters the body) and its elimination (how it is removed from the body). FOF ¶ 126. Working backwards, a drug is removed from the body through elimination when it is either broken down (*e.g.*, by enzymes in the liver) or urinated. FOF ¶ 176. While the rate of elimination may vary to some degree between different people, it is generally fixed for a given individual. *Id.* Put simply, no matter how a drug enters the bloodstream, it will be removed at a certain pace. *Id.*

That fixed rate is not the case for the absorption of the drug. The absorption rate can be changed by manipulating the way the drug is delivered to the body. FOF ¶¶ 149-51, 154. There are myriad ways in which drug delivery can be altered, thereby impacting the absorption profile in order to obtain a desired drug concentration. These include delivery mechanisms (oral v. injectable), formulation ingredients (also known as excipients), and the drug's physical characteristics (*e.g.*, particle size). *Id.*; *see also* FOF ¶¶ 496-98. Experts for both parties agree that each of these characteristics can impact the pharmacokinetic profile of a given drug such that different preparations or delivery of the same drug molecule can yield significantly different pharmacokinetic profiles. FOF ¶¶ 483-88; 496-98. Alternatively, if the same delivery mechanism and same (or nearly the same)

formulation are used, then pharmacokinetic profiles for one extended release formulation may be used to reasonably predict the pharmacokinetic profile of a longer extended release formulation. FOF ¶¶ 174-76, 178, 194. For example, Invega Sustenna® was formulated such that, instead of all of the drug being absorbed at once, the drug was absorbed relatively slowly over time. FOF ¶¶ 127, 328. This formulation is known as a depot formulation because it involves injecting a larger dosage of a drug (as compared to a daily administration) into a large muscle, such as the deltoid or gluteal. *Id*. at ¶¶ 154-55. Because of how the drug is formulated, it is absorbed into the bloodstream slowly such that one-dose administration can last a patient up to a month. FOF ¶¶ 142-43. As such, it is referenced as a long-acting injectable or "LAI."

POSAs are well-versed in how to manipulate the absorption rate because it was demonstrated in the well-known work of Hirano. FOF ¶ 151, n. 4; DTX-020 (Hirano). Specifically, the absorption rate of a drug with poor solubility can be controlled through manipulation of the drug's particle size. *Id*. at ¶¶ 151-53. For a given amount of drug, the larger the particle size, the slower the absorption will be. FOF ¶ 151. That is because a larger molecule will have a smaller ratio of surface area to volume; essentially, the outer portion of the molecule is the part that is primarily being dissolved, and for larger molecules it takes longer to get to the

center.[15] FOF ¶¶ 151-53. Based on these teachings, a POSA would expect that increasing particle size would extend the absorption of a drug. *Id*. at ¶ 151.

Another aspect of pharmacokinetics known to a POSA at the priority date was "flip-flop" pharmacokinetics. Flip-flop pharmacokinetics reflect whether it is the absorption or elimination of a drug that predominantly impacts its concentration and duration in the bloodstream. FOF ¶¶ 162-64. In an immediate release formulation, the drug is absorbed very quickly and the time it stays in the body is primarily dependent on elimination pathways. That is what is termed "normal" pharmacokinetics. *Id*. at ¶ 163. Flip-flop pharmacokinetics are essentially the opposite: the drug gets absorbed as it dissolves over an extended period of time and this rate of absorption controls the concentration of the drug in the body, especially in the early phase after dosing. *Id.* at ¶164.

So far, the background knowledge of a POSA on pharmacokinetics has focused on how absorption or elimination can (or cannot) be impacted by different variables. However, a POSA would also know how to monitor or measure the concentration of a drug as it is absorbed and/or eliminated. FOF ¶¶ 125-26, 129, 174. That can be done using Cmax (the point on a plasma curve at which the rates of elimination and absorption of a given drug meet or the maximum concentration of drug in the body following an injection), Tmax (the time point at which Cmax is

[15] FOF ¶¶ 152-53 (detailing sugar cube analogy).

reached on a plasma curve), and AUC (the area under the plasma curve that corresponds to the amount of exposure a patient has to a given drug). FOF ¶¶ 134-36. And one parameter of particular relevance to this case is half-life.

The half-life is the amount of time that it takes for half of the drug in the body to be removed from it. FOF ¶ 137. It is common—and holds true for paliperidone—that the half-life is on a logarithmic scale, also referred to as first order. FOF ¶ 138. The drug is eliminated from the body in the following manner: 1 half-life = 50% of the drug remains; 2 half-lives = 25% of the drug remains; 3 half-lives = 12.5% of the drug remains; 4 half-lives = 6.25% of the drug remains; 5 half-lives = 3.25% of the drug remains; etc. FOF ¶ 139. Once a patient gets past one to two half-lives, the amount of drug left in the system is significantly reduced. By three half-lives, nearly 90% of the drug has left the system. *Id.*

Because of this underlying principle, the half-life of a drug formulation often correlates with the recommended dosage interval. That is, the dosage interval for a chronic condition that requires continued treatment is usually going to be around one to two half-lives, as anything longer than that would lead to the patient having insufficient drug concentrations in the system. FOF ¶ 140. The prior art LAI formulations reflected this common theme. As described in the '536 Publication for all depot antipsychotics, the administration interval was in the range of about one to two half-lives. FOF § XI.A; DTX-97.0019; FOF ¶¶ 144, 181.

3. Scope of the Prior Art: the Invega Sustenna® Product, a *Specific* PP1M Formulation FDA-Approved for the Treatment of Schizophrenia

These established pharmacokinetic properties were utilized in the prior art development of Invega Sustenna®. Invega Sustenna® was approved by the FDA in 2009 for the safe and efficacious treatment of schizophrenia. To be sure, the prior art discloses a variety of potential PP1M formulations. FOF ¶ 490. But, of all the different formulations disclosed, only two nearly-identical ones were disclosed as used in clinical trials—one of which was the specific formulation the FDA approved as Invega Sustenna®. FOF ¶ 490-91.

The pharmacokinetic results of clinical testing of those two formulations were disclosed in prior art Samtani 2009 and were referred to as F011 and F013. FOF § XI.G; DTX-045.0003. Though Samtani 2009 does not disclose the specifics of those formulations, they are publicly disclosed in the Janssen '519 Publication. FOF § XI.B. Specifically, at Table 2, the '519 Publication describes the F013 formulation, which has specific ingredients at specific concentrations: paliperidone palmitate, polysorbate 20, citric acid, disodium hydrogen phosphate and sodium dihydrogen phosphate, sodium hydroxide, Polyethylene Glycol 4000, and water for injection. DTX-007.0012. This same section of the '519 Publication also discloses the F011 formulation; it is the same as F013 except that the citric acid and sodium hydroxide ("NaOH") are not present. DTX-007.0012 at [0064].

The specific formulation that was actually FDA approved in the Sustenna Label is the same as the F013 formulation of Samtani 2009 and the '519 Publication. *See* FOF ¶ 328; DTX-025.0038. In addition to the formulation information, both the '519 Publication and Sustenna Label provided information about what to do if a patient misses a dose of that formulation. FOF ¶ 344. In light of the results of the clinical trials in Samtani 2009 and the FDA approval of one of the two formulations therein, a POSA would know that two specific PP1M formulations can be utilized to treat schizophrenia and in a missed dosing regimen. FOF ¶ 490. But a POSA would not conclude that all of the potential PP1M formulations would work because, as described above, a POSA would know that changing variables (*e.g.*, the ingredients of the formulation) can change the pharmacokinetics of the formulation. *Id.* at ¶ 491. As just one example, the '843 patent (incorporated by reference into the '693 patent) discloses a PP1M formulation with paliperidone palmitate having an average particle size (d50) of greater than or equal to five microns. FOF ¶ 233, 489. That is in direct contravention of the '693 patent, which states that such a d50 would be expected to result in a PP3M formulation, not a PP1M formulation. *Id*.

4. Scope of the Prior Art: Missed-Dose Regimens

Having a missed-dosing regimen for an LAI was not a novel concept as of the priority date. FOF ¶ 344. As noted above, the Sustenna Label specifically addressed "missed doses" for the FDA approved PP1M formulation. But that was

not even novel for paliperidone palmitate specifically. For instance, the '536 and '519 Publications also disclose missed dose information for PP1M. FOF ¶ 344.

When a patient is taking a drug as directed, the drug's concentration within the body is expected to be at a steady state within the therapeutic window for that patient. FOF ¶¶ 168-69. When the patient misses a dose, the body's elimination mechanisms continue to work and the concentration of the drug continues to fall. That is why the prior art missed-dose information was, and continues to be, guided by the drug's pharmacokinetics with the goal of reaching steady state quickly. FOF ¶¶ 384, 388-97. That is where half-lives come in; as each half-life passes without further administration of the drug, the concentration of the drug within the body is halved. FOF ¶¶ 139-40.

The prior art missed-dose information related to PP1M universally applied a three-window approach. FOF ¶ 344. The first window is for patients who recently missed a dose and, as a result, likely have not passed even one additional half-life. FOF ¶¶ 385-86. Because more half-lives have not passed, the drug concentration of such a patient is going to be only slightly less than the steady state level. For this patient, the prior art teaches resumption of normal dosing (*i.e.*, without reinitiation loading doses). *Id*. Specifically, there, the prior art taught that within six weeks of the last one-month dose, the patient can just resume normal maintenance dosing (*i.e.*, within two weeks from when the dose should have been given). *Id*.

On the opposite end of the spectrum is the third or last window for patients who have not taken a dose for a long period of time. *Id*. Unlike their first-window counterparts, these patients are likely to have passed through several half-lives. As noted above, after several half-lives, a POSA would expect the drug concentration to be minimal. With no drug in the system, pharmacokinetically it is akin to these patients having never taken a dose in the first place (which is also called treating the patient as "naïve"). *Id*. The Sustenna Label, '536 Publication, and '519 Publication (collectively, "PP1M Prior Art") taught that treatment for such patients should be started anew. *Id*.; *see id*. ¶ 413.

In the middle are patients who have missed a dose for an interim period of time. For these patients, the first missed-dose window is insufficient because too much drug has been eliminated but, also, treating the patient as naïve would provide too much drug. As taught by the PP1M Prior Art, and general pharmacokinetic principles, a second or middle window is needed for these patients

a) Specific Missed-Dosing Regimens of the Prior Art Included a Middle Window

Each of the PP1M Prior Art references teaches the same parameters for the middle window as described above. They disclose administering two loading doses a week apart followed by resuming the patient's previously stabilized monthly maintenance dose of PP1M. FOF ¶ 349. A loading dose is generally a larger dose of a drug, either given in single or multiple doses, designed to spike a patient's drug

concentration up to a therapeutic level that may then be managed by continuing maintenance doses. Loading doses were well known to POSAs given their prevalence in initiation and reinitiation drug regimens. FOF ¶¶ 159, 161. The PP1M Prior Art taught that the first loading dose should be given as soon as possible following the missed dose. FOF ¶ 351. The second loading dose should be given about a week after the first loading dose. FOF ¶ 353 Then the patient should be given the previously stabilized maintenance dose about a month after administration of the loading doses. FOF ¶ 355.

The PP1M Prior Art teaches the timing of doses as well as their location. Each PP1M Prior Art middle-window dose regimen teaches administering the two loading doses in the deltoid before going back to the maintenance dose. FOF ¶¶ 349, 357. And the PP1M Prior Art teaches the strengths of the loading doses, *i.e.*, use the same dose amount the patient was previously stabilized on, except for the highest dosage in which the loading doses should be the second highest. FOF ¶ 363.

b) Timing of the Middle Window

The PP1M Prior Art is consistent regarding the timing of the middle window. The middle window is aimed at patients who no longer have enough drug in their system to be at steady state but who still have some drug present in their body such that they cannot be treated as naïve. FOF ¶ 386. Each of the Sustenna Label and

the '519 and '536 Publications set the middle window from six weeks to about six months since their last dose. FOF ¶¶ 345-48.

The Sustenna Label also described certain clinical trials that Janssen conducted with PP1M including a minimum 12-week, fixed-dose stabilization phase, and a randomized, placebo-controlled phase to observe for relapse. FOF ¶ 414; DTX-25.0046-47. During a double-blind phase, which began after patients were all stabilized on PP1M, patients were randomized to either the same dose of Invega Sustenna® that they had received during the stabilization phase or to a placebo. *Id.* This study taught that the median time to relapse for the placebo group was 193 days from time point zero (*i.e.*, the point at which a patient in the study received the placebo instead of the one-month formulation). FOF ¶ 411.

5. Scope of Prior Art: A Specific PP3M Formulation was Successful in Phase III Clinical Trials per JAMA and Other Art Not Before the USPTO

Janssen conducted a Phase III clinical trial to "evaluate the efficacy and safety of [PP3M] vs. placebo" in treating schizophrenia. Janssen detailed the results of this clinical study in the JAMA article.[16] Janssen did not disclose JAMA

[16] JAMA was not just a one-off publication either. The JAMA article spans 78 pages and includes all aspects of trial design, including the clinical protocol (*e.g.*, inclusion, exclusion, demographics, and discontinuation of treatment). DTX-026. It was also presented publicly ahead of the priority date (by a non-inventor) at a public forum and highlighted in Medscape. *See* DTX-109.0001-0004.

to the USPTO during the prosecution of the '693 patent and, for most of the litigation contended that it was not prior art.[17] Until Janssen could no longer deny that JAMA was prior art, it had good reason to try to brush it aside. JAMA teaches about the relationship between treating schizophrenia with both a PP1M formulation and a PP3M formulation that, in combination with the prior art discussed above, renders the claims obvious.

JAMA discloses a clinically successful protocol where a patient is initiated (and stabilized) on specific PP1M doses, and then is converted to a specific PP3M dose. FOF ¶¶ 364-66. As such, JAMA teaches a POSA a conversion between equivalent PP1M and PP3M doses and provides the specific values for doing so. *Id.*; *see also id.* ¶ 368. Further, JAMA was a placebo-controlled study where some patients received the active PP3M while others received a placebo with no medicine. FOF ¶¶ 398-400. Because the placebo patients received no medicine, a POSA would know that such patients mimic those outside of a trial who would miss doses. *Id.*

JAMA also contained both an interim analysis—which the authors said was primary—and final analysis. FOF ¶ 401. Thus, a POSA would know to rely on the interim (or primary) analysis and related data. *Id.* The interim analysis found that "sufficient patients had reached efficacy compared to placebo." *Id.* The interim

[17] Janssen conceded it was prior art shortly before trial. D.I. 99, SOF at ¶ 52.

analysis also looked at relapse information in both the PP3M treatment and placebo groups. The relapse information for the placebo group recounted what happened to patients at different time intervals after taking the last dose of the drug, similar to the way the Sustenna Label reported relapse information for PP1M clinical trials. FOF ¶ 411. Specifically, Figure 2 reports information based on the days since the patient missed a maintenance dose. Because a patient *misses* a maintenance dose 90 days after taking the last dose, adding 90 days to Figure 2 reflects the amount of time since a patient was last *administered* a dose in the parlance of Claim 5. The interim analysis showed median time to relapse for patients was about 364 days (274 days in the figure, plus 90) or about a year. FOF ¶ 402; *see* DTX-026.0006. The data further showed that, at that 360-day interval, there was a wide "confidence interval" such that as many as 80% of patients could expect to relapse within a year of missing a dose.

The JAMA article was not the only place Janssen described treating schizophrenia with a combination of PP1M and PP3M. NCT '423, another prior art publication, also provided equivalents between PP1M and PP3M doses to account for the differences in dosing intervals (between one- and three-months). FOF § XI.E (DTX-021); *id*. at ¶ 375. NCT '423 detailed a Janssen clinical trial testing whether patients could be stabilized on PP1M and then converted to PP3M. FOF ¶ 374. While NCT '423 did not detail the results of this study, such results can be found in the 2014 Press Release, where Janssen lauded the successful results

and indicated that Janssen halted the trial early. FOF § XI.F (DTX-027); *id*. at ¶ 376. A POSA would understand that Janssen's ending of the study early was a rare step, taken only when a "strong conclusion" was already reached. *Id*. at ¶ 376.

Despite Janssen's obligation to do so, it did not disclose any of the pieces of prior art discussed in this section to the examiner during prosecution of the '693 patent. FOF ¶¶ 371, 377. A patent applicant has a duty to disclose information material to patentability to the examiner. *See* 37 C.F.R. 1.56 ("Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the [USPTO], which includes a duty to disclose to the Office all information known to that individual to be material to patentability . . . ."). The examiner did not disclose finding any of these prior art publications through independent searches, either. FOF ¶¶ 371, 378.

Janssen of course knows this. And, that is why it attempted to cloud the issue by suggesting the examiner "may" have seen the aforesaid references, but did not present anything but imaginative speculation (not evidence). FOF ¶ 371-73, 378. To be sure, nothing in the record supports Janssen's supposition. It must be disregarded. *Cf. Sun Pharma Global Fze v. Lupin Ltd.*, 2021 WL 856886, at *4 (D.N.J. Mar. 8, 2021) (noting an expert could not opine on the examiner's search history because he "plainly lack[ed] personal knowledge" of it); *Rohm & Haas Co. v. Crystal Chem. Co.*, 722 F.2d 1556, 1573-73 (Fed. Cir. 1983) (finding a presumption the examiner found critical information was not proper given the

"mountain of largely irrelevant data" before the examiner and the real-world conditions of examiners at the USPTO). Because critical art was not before the patent office, no deference is owed. *Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. 91, 111 (2011). This is particularly true given that, in advocating for allowance of the patent, Janssen argued before the patent office that "[i]t is not the situation where one can just do 3x whatever was done for PP1M to get an idea of what to do for PP3M." DTX-008.0216. That may be true. But, the conversion between PP1M and PP3M was disclosed in prior art like JAMA. And that art was not put before the patent office.

B. What a POSA Would Have Done in April 2015 Based on the Prior Art, and How that Renders the Asserted Claims Obvious

Against this backdrop, the Asserted Claims are obvious. Section 103 ensures that "the results of ordinary innovation are not the subject of exclusive rights under the patent laws." *KSR*, 550 U.S. at 427. "Were it otherwise, patents might stifle, rather than promote, the progress of useful arts." *Id.* (citing U.S. Const. art. I, § 8, cl. 8). Furthermore, patents "should not be irrebuttably presumed valid" because of "the public interest support[ing] judicial testing and elimination of weak patents." *In re Thalomid & Revlimid Antitrust Litig.*, Case No. 14-cv-6997, 2015 WL 9589217, at *13 (D.N.J. Oct. 29, 2015) (quoting *King Drug*, 792 F.3d at 398 (alteration in original) (citation and internal quotation marks omitted)).

Courts evaluate a patent and the prior art through the lens of a POSA, who is

a hypothetical person presumed to know all of the relevant art. *In re GPAC Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995); *Union Carbide Corp. v. Am. Can Co.*, 724 F.2d 1567, 1576 (Fed. Cir. 1984) (describing the POSA as "the inventor working in his shop with the prior art references—which he is presumed to know—hanging on the walls around him."). Of particular importance, when evaluating obviousness, courts note that a POSA is not an "automaton" but instead possesses "ordinary creativity." *KSR*, 550 U.S. at 420-21. As such, a POSA can fit the disclosures of multiple prior art publications together "like pieces of a puzzle." *Id.* When a patent utilizes a dosage that is FDA approved for the same purposes as described in the prior art, it is obvious. *See In Re: Copaxone Consol. Cases*, 906 F.3d 1013, 1027 (Fed. Cir. 2018).

1. With a Safe and Effective PP3M Treatment Disclosed by JAMA and an FDA-Approved PP1M Formulation, a POSA Would Have a Reasonable Expectation in a Working PP3M Formulation

The obviousness analysis focuses on what was known at the time of the invention. Here, there was a host of information regarding not only PP1M, but PP3M. The Sustenna Label, which was approved by the FDA, taught that a PP1M formulation could be used to treat schizophrenia and was utilized in the field since 2009. FOF ¶¶ 181, 184, 328. PP3M, JAMA, and NCT '423—as informed by the 2014 Press Release—taught that a PP3M formulation could be safely and effectively used to treat schizophrenia. FOF ¶ 380. In addition to these prior art

teachings on the efficacy of both PP1M and PP3M formulations for schizophrenia, a POSA would also understand general pharmacokinetic principles including basic teachings from Hirano, a standard textbook in the field. FOF ¶ 151.

Hirano taught that the particle size of a drug formulation affects the body's absorption of a drug. *Id*. Indeed, a POSA seeking to slow absorption and ensure that a drug lasts for three months in a patient's body rather than one month would know that making a drug's particle size larger could accomplish this goal. *Id*. That is why a POSA would have no trouble taking the one formulation disclosed as Invega Sustenna® and manipulating the particle size to arrive at an otherwise similar three month formulation. FOF ¶ 492.

Janssen does not appear to dispute this point. Janssen of course did not present the testimony of a formulator on the issue of obviousness. Further, evidence showed that Janssen did exactly what a POSA would have done in light of the prior art: [redacted] Moreover, there is no evidence that rebuts Dr. Forrest's reasonable and supported opinion that a POSA would be able to design *a* PP3M formulation that could be utilized in the claimed dosing regimen given the teachings of the prior art.

2. JAMA's Safe and Effective PP3M Treatment, Would Have Motivated a POSA to Develop a Missed-Dosing Regimen Analogous to the PP1M Treatment

A POSA knowing the dosing regimen in JAMA would have also determined missed-dosing information. Janssen did not seriously dispute that a POSA would be motivated to develop a missed-dosing regimen for a PP3M product. And how could they? At the time, the PP1M Prior Art each included missed-dosing information for PP1M, so a POSA would be motivated to develop analogous information for PP3M. *See In Re: Copaxone*, 906 F.3d at 1025-26 ("The potential for FDA approval also may properly be considered, as it was here, in determining whether one of ordinary skill would be motivated to develop a drug product[.]") (internal citations and quotations omitted); *see* FOF ¶¶ 381-82. The PP1M missed-dose regimens were based in part on general teachings and calculations about paliperidone palmitate, which a POSA would use for PP3M missed-dose regimens as well. FOF ¶ 384; *see Anacor Pharms., Inc. v. Iancu*, 889 F.3d 1372, 1384 (Fed. Cir. 2018) ("Where the patent is directed to a new treatment using a known compound, it is reasonable to assume that similar compounds that share certain common properties are apt to share other related properties as well."). Drs. Forrest and Sommi both testified that a POSA would consider PP1M missed-dose prior art including the '536 and '519 Publications to determine missed-dose information for a long-acting injectable paliperidone palmitate product, such as PP3M. *Id*. Further, JAMA disclosed an initiation regimen for PP3M that was proven to be safe and

effective, and it included a table for corresponding PP1M and PP3M doses. FOF ¶¶ 386, 418. These teachings combined would motivate a POSA to devise PP3M missed-dose information.

3. Using the Prior Art, a POSA Could Develop Three Dosing Windows for a PP3M Formulation to Address Varying Patient Dosings

Because of the general teachings about paliperidone palmitate incorporated in the PP1M Prior Art, a POSA would be motivated to use the same three missed-dose windows. Each of the Sustenna Label, the '519 Publication, and the '536 Publication teach three missed-dose windows. FOF ¶ 304. The first window is from just after a patient misses a dose of PP1M until about two weeks since the missed dose (or six weeks since the last drug administration). FOF ¶¶ 385-86. The second window, or the middle window, covers from about six weeks to about six months since the last administered dose. FOF ¶¶ 345-47. The third and final window covers when a patient has missed a dose and was last administered one more than six months ago. FOF ¶¶ 385-86.

A POSA would understand that a patient who misses a dose of PP3M still has some amount of the drug present in their body, which is continually being eliminated. FOF ¶¶ 168, 176. General pharmacokinetic principles teach that the amount of drug present after a maintenance dose of a drug depends on the time since injection and elimination and absorption rates, among other factors. FOF ¶¶ 125-26. A POSA could use equations taught by the prior art to calculate the start

and endpoints of these missed-dose windows. FOF ¶¶ 129, 387. But the POSA was not limited to only general pharmacokinetic principles and mathematical equations here: the PP1M missed-dose regimens each set forth missed-dose windows, elaborated *supra*.

4. The Dosage of the Middle Window Would be the Same as for Invega Sustenna® PP1M

A POSA would understand that the therapeutic needs of a patient in the middle window for either the PP1M or PP3M missed-dose regimen were similar. The goal of treatment with an LAI such as paliperidone palmitate is to keep a patient within a steady-state range. FOF ¶ 160. A patient is in this range when there is enough drug in their system to maintain a therapeutic concentration with regular maintenance doses. FOF ¶ 158.

There is no difference in the drug concentration in the body for patients in the middle window regardless of whether they were being treated with PP1M or PP3M; in each case the patient would have some amount of the drug remaining in their body, but not enough; it would be below steady state. FOF ¶¶ 385-86. The prior art teaches a specific dosing regimen for patients who have some but not enough drug in their system—*i.e.*, the middle dosing window that was already on the FDA-approved Sustenna Label. A POSA would select that dosing regimen for the analogous patients in the PP3M middle missed-dosing regimen and have a reasonable expectation that it would work. *See In Re: Copaxone,* 906 F.3d at 1026

(finding claimed dosage invalid where there was potentially an "unlimited" "universe of dosages" but only two had clinical support as safe and effective: 20 mg and 40 mg"). Here, the claimed dosing range is even more obvious than that in *In Re Copaxone* because there was only one missed-dosing regimen for patients in the middle window with some but not enough paliperidone in their systems.

Because such a patient's drug levels would be lower than the steady-state range, a POSA would follow the teachings of the PP1M Prior Art of using two loading doses to quickly get the patient back up to the steady-state range of paliperidone palmitate. FOF ¶¶ 389, 349-50. That motivation to use PP1M as the loading dose was established by both JAMA and NCT '423, which taught a POSA that all loading doses for PP3M are PP1M. FOF ¶¶ 365, 374. Following reinitiation of the patient back into steady state using these loading doses, a POSA would then resume maintenance doses of PP3M—exactly what was done with the PP1M product. FOF ¶¶ 389, 355-56. And those exact dosages were provided by JAMA. FOF ¶¶ 366-68.

5. Timing of the Middle Window Would be Reasonably Understood to be in the Range of Four to Nine Months

The PP1M Prior Art taught a middle window of between six weeks and six months. This window timing was for a PP1M product, so a POSA would know that it should be lengthened for a PP3M product. That is because a PP3M product would be expected to have a longer half-life corresponding to the longer dosage

interval. *See supra*, § 111.A.2 (detailing how a POSA would understand the relationship between half-life and dosing interval for LAI formulations). In determining the middle dosing interval for the PP3M product, the POSA would consider all of the teachings of the prior art, not just one specific piece of prior art in isolation.

On the front end of the middle-dosing interval, the prior art consistently pointed toward about four months. For the PP1M product, the front end of the middle-dosing window was six weeks. This six week period was about 1.4 times the dosing interval for the PP1M product of 30 days, which in turn was tied to the approximate half-life. FOF ¶¶ 388-90. As such, patients in that range would be approaching the second half-life of the drug and, thus, would likely have significant amounts of drug in their system, albeit below steady state. Dr. Forrest testified that it would be reasonable for a POSA to utilize the same ratio for the PP3M product. FOF ¶ 391. Using that ratio of 1.4 times the dosing interval of three months, a POSA would expect that approximately four months from the initial dose would be an appropriate beginning of the middle window. *Id*. (1.4 x 90 days = 126 days, or 4.2 months). At the time, there were no countervailing clinical considerations or other prior art, so a POSA would determine four months to be appropriate and have a reasonable expectation that it would work.

Determination of the back end of the middle-dosing window also involved consideration of all of the prior art, which is precisely what Dr. Forrest did. One

input was, again, the PP1M Prior Art missed-dosing information. There, the backend of the middle-dosing window was six months, which is six times the dosing interval. Multiplying that window by the PP3M dosing interval gives a backend of 18 months. FOF ¶¶ 392-94.

But a POSA would recognize that 18 months is a significant amount of time without a dose and, further, that it would correlate to a number of half-lives such that the patient would likely have little paliperidone in the system for several months. FOF ¶¶ 392, 395. The POSA would understand that relapse rate is a significant risk for these types of patients and relevant to determining the back end of the middle window. FOF ¶¶ 395, 397. Notably, all experts at trial agreed that preventing relapse is a main goal of schizophrenia treatment. FOF ¶¶ 107. And, here, a POSA had two sets of relapse rate information to consider: that provided for the PP3M in JAMA and that provided for PP1M in the Sustenna Label.

As discussed *supra*, the primary analysis of JAMA—namely, the interim analysis—taught that the median time to relapse was 364 days after the last dose, which is about four half-lives. FOF ¶ 402-03, 405. But because of statistical variance, at this time period, up to 80% of patients could be falling into relapse. FOF ¶ 404. Therefore, a POSA would not want to wait that long until beginning a full reinitiation dosing for naïve patients. The "natural jump" from this conclusion would be to set the endpoint one half-life earlier: at three half-lives. FOF ¶ 406. This endpoint would be nine months for PP3M. *Id*. at ¶ 407. That is just what the

JAMA data would teach: at the 9-month date (180-days on the x-axis of Figure 2, which is 270-days from the last dose), the interim analysis discloses that about 60-70% of patients are being effectively treated and have not relapsed. FOF ¶ 408-09. So, given the combination of prior art and general knowledge, a POSA would arrive at the claimed window of four to nine months.

This approach—considering the relapse rate—is also supported by the prior art teachings from the Sustenna Label. That label included a similar relapse rate analysis, but for the PP1M product. *See* DTX-025.0047, at Figure 1. A POSA would know from reviewing Figure 1 that, at 193 days since a patient's last dose (163 days for the median time to relapse for the placebo group plus 30 days to account for the period of time since the patient received PP1M), a significant number of patients would have relapsed. FOF ¶ 411. From that knowledge, a POSA would understand that the end of the middle-dose window should be set earlier than that median time to relapse. FOF ¶ 413. That is why the prior art teachings from JAMA and the Sustenna Label would lead a POSA to optimize the end point of the middle window from a maximum of 18 months down to nine months. FOF ¶¶ 406-07.

Though the prior art alone—without any pharmacokinetic modeling—would lead a POSA to a four-to-nine month middle window, Mylan's expert, Dr. Forrest, conducted pharmacokinetic modeling to validate that position, especially as to the nine-month endpoint. *See* FOF § XII.A.6. To create his modeling, Dr. Forrest

relied on the prior art mentioned above, including both well-established pharmacokinetic principles and numerous disclosures specific to paliperidone (including JAMA) and the Samtani 2009 publication. *Id*.

Samtani 2009, published by Janssen, provides pharmacokinetic data, including population PK ("popPK") data, for two PP1M formulations. FOF ¶ 341. The article outlines models based on data taken from actually administering those two specific PP1M formulations. However, it does not provide the underlying data. FOF ¶ 432. While the details of the model are somewhat complex (in order to meet the demanding standards of FDA approval), for the purposes of Dr. Forrest's creation of a model to *approximate* the end of the middle-dosing window, Samtani 2009 taught that the PP1M formulation pretty much followed normal flip-flop kinetics: 83% of absorption and 100% of elimination followed usual first-order kinetics. FOF ¶ 433. While 17% of absorption was a faster zero-order process, this did not impact the purpose of Dr. Forrest's modeling, which was to look at the expected plasma levels of a patient after missing a dose for several weeks. FOF ¶¶ 433, 436.[18] That is because, by day 15, the intramuscular profiles showed a monoexponential delay (*i.e.*, followed the 83% first order) which defined the half-life of the product. FOF ¶ 433. Indeed, Dr. Forrest validated his model by comparing it to the actual plasma levels reported in Samtani 2009. And, to no

[18] Dr. Forrest further explained that the 17% is incorporated in his model; it is simply that the rate of absorption of that 17% is different. FOF ¶ 433.

surprise based on the level of ordinary skill in the art, Dr. Forrest's model is spot-on during the relevant time period. FOF ¶ 436.

Once his model was created and its efficacy validated, Dr. Forrest could test different multipliers of the PP1M dosage form to predict efficacy of PP3M within the claimed dosing window. *Id*. Using the model, Dr. Forrest validated that a 3.5-times dose of the PP1M dosage form, or 350 mg. eq. of PP3M, provided efficacy through at least 90 days. FOF ¶¶ 435-36. In that respect, Dr. Forrest was able to confirm that his modeling aligned with the teachings of JAMA. FOF ¶¶ 434, 437. At the four-month point, a patient given this PP3M strength would be in the therapeutic range. FOF ¶ 436. At nine months since the last injection, the patient's drug concentration would be just about to dip below therapeutic efficacy. *Id*. Therefore, Dr. Forrest's pharmacokinetic model check validated his opinions based on the other prior art. *See* FOF ¶¶ 436-442 (citing DTX-197).

In response to Dr. Forrest's testimony, Janssen presented the testimony of Dr. Gobburu. Dr. Gobburu conceded that popPK modeling was just one tool that a formulator could utilize to develop a dosing regimen. FOF ¶ 180. But on the issue of Dr. Forrest's modeling, Dr. Gobburu's testimony had several fatal flaws which made his opinions unpersuasive. First, he did not put himself in the perspective of a *hypothetical* POSA even when considering the limited art he did review. FOF ¶ 57-8; *In re GPAC Inc.*, 57 F.3d at 1579. Second, he did not consider most of the pertinent prior art in this case including key pieces of paliperidone-

specific references which informed on Dr. Forrest's modeling and calculations (such as JAMA). FOF ¶ 58. Nor did Dr. Gobburu find it pertinent to review the entirety of the '693 patent, including the Asserted Claims. FOF ¶ 59. Given that Dr. Gobburu failed to provide his opinions from the perspective of a hypothetical POSA and did not consider the available prior art (or even the entirety of the patent-in-suit), his opinions carry limited weight.

6. Following the Prior Art, a POSA Would have been Motivated to Develop the Claimed Dosing Regimen with a Reasonable Expectation of Success

Obviousness is determined by comparing the teachings of the prior art to the claimed invention as a whole, but it is appropriate to consider specific elements in reaching that determination. *See In Re: Copaxone,* 906 F.3d at 1026-27. Here, how to treat a patient that misses a dose and returns for treatment in the four-to-nine month window since his or her last injection amounts to no more than a POSA "fit[ting] the teachings of multiple patents together like pieces of a puzzle." *KSR*, 550 U.S. at 420.

Under the PP1M Prior Art, when a patient suffering from schizophrenia comes in for treatment and is likely to have some but not a sufficient amount of paliperidone in her system (misses a dose and returns after a moderate period of time), the FDA-approved dosing regimen to get the patient back into the steady state is: (i) deltoid shot of PP1M immediately; (ii) deltoid shot of the same dose of PP1M one week later; and (iii) back to the previous maintenance dose one month

later. The use of these exact same three steps found in the PP1M Prior Art to treat the same type of patient is obvious. *In Re: Copaxone*, 906 F.3d at 1027 ("this court has previously employed the same frequency-and-dosage-amount approach to obviousness used by the district court here"). All that is left is the amount of each dose to be used. And a POSA could have derived that dosage using the conversion from PP1M to PP3M as taught in JAMA (a clinical trial that was so successful that it was stopped early to be fair to those taking the placebo). FOF ¶ 376. Combining such prior art, a POSA would have had a reasonable likelihood of success in arriving at the claimed dosing regimen which, therefore, was obvious.

The main dispute at trial was the contours of the middle four-to-nine month window. For the reasons stated in Section III.B.5, a POSA would have arrived at exactly that window. But where the parties' disagreement lies is also an important issue. Janssen's expert, Dr. Sommi, offered that the prior art would have led a POSA to a window of somewhere around five to six months as a starting point and eighteen months as an end point. FOF ¶ 410. He also seemed to suggest that there was nothing particularly inventive about this window (for infringement purposes), opining that the window is a mere "clinical descriptor." FOF ¶¶ 279-80. Whether applying Dr. Sommi's range or Dr. Forrest's range, there is agreement that patients returning between five or six months to nine months would fall within the middle window. FOF ¶ 410. For those patients in the five/six to nine month window, Dr. Forrest credibly testified that the way to treat such patients based on the prior art

teachings would be administering two injections of PP1M in the deltoid a week apart and returning to the PP3M maintenance dose a month later. FOF ¶ 351.

But, on that point, identifying the beginning and end point outside of the agreed upon five or six to nine month middle window requires no more than routine optimization for a POSA. And it is well-settled that "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456 (C.C.P.A. 1955) (citations omitted); M.P.E.P. 2144.05.II.A. In fact, a *prima facie* case of obviousness usually "exists when the ranges of a claimed composition overlap the ranges disclosed in the prior art." *E.I. DuPont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1006 (Fed. Cir. 2018); *see* COL ¶ 59 (collecting cases). This overlap leads to a presumption of obviousness. *Id*.

Such a presumption of obviousness is appropriate here where the experts on both sides agree that the prior art teaches a range of, at the very least, five or six to nine months for a middle window. Whether based on Dr. Forrest's opinions that the prior art taught the four-to-nine month window exactly or the precedent regarding overlapping ranges between what is taught by the prior art and the claimed range, the claim is invalid.

7. Janssen's Manufactured Distinctions Between the Prior Art and Claimed Invention Do Not Support a Finding of Non-Obviousness

At trial, Janssen disputed obviousness by repeatedly resorting to a slide contending that four elements were missing from the prior art: (1) a missed dose regimen for PP3M, (2) the four-to-nine month patient population, (3) using PP1M after a patient advanced to PP3M, and (4) using PP3M without stabilizing with four or more months of PP1M. Tr. 538:2-20 (Sommi). This argument is does not save the claim because "non-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references." *In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986), as cited in *Soft Gel Technologies, Inc. v. Jarrow Formulas, Inc.*, 864 F.3d 1334 (Fed. Cir. 2017). Factually, a POSA would have arrived at the claimed subject matter based on the teachings of the prior art. What Janssen claims as a "unique combination" is no more than the result of the prior art teachings of PP1M missed-dose regimens and PP3M prior art which was never disclosed to the patent office.

A missed dose regimen for PP3M: Janssen's reliance on this point only underscores how far it has to reach to try to rebut the strong obviousness case here. Of course, the claimed missed-dose regimen for PP3M is not in the prior art. If it were, the claims would be anticipated and invalid under 35 U.S.C. § 102—a defense Mylan did not raise in this case. But a nearly identical missed-dose regimen *did* exist in the prior art related to PP1M and, naturally, a POSA

developing a PP3M product would use the known techniques from PP1M and apply them in the same way. *KSR*, 550 U.S. at 416. That is exactly what Dr. Forrest did. FOF ¶ 384-85.

The four-to-nine month patient population: It should not go unnoticed that, for the purposes of infringement, Janssen does everything it can to argue that the four-to-nine month portion of the preamble is simply a "clinical descriptor" of who the claimed methods are applied to. Yet, for invalidity, Janssen transforms that time frame into the proverbial golden goose, arguing that that no POSA would be able to determine that claim element absent thousands of clinical data points. FOF ¶ 50. That cannot be; Janssen cannot have it both ways. But, if Janssen is correct that this is not a step of the claim but remains an element that Mylan must prove is invalid, the prior art would have led a POSA to this four-to-nine month window. *See* Section III.B.5.

Using PP1M after a patient advanced to PP3M: Janssen's argument here, again, overreaches in the required proofs. Mylan concedes that no prior art disclosed *exactly* what is claimed in the '693 patent. But that is not the test for obviousness. The test is whether a POSA would have been led by the prior art to the claimed subject matter. Here, the prior art taught that the FDA approved PP1M as a dosage that could be used as loading doses for a patient that missed a previous maintenance dose and was at risk of drug concentration dipping below the previous steady state. FOF ¶ 370. Whether the previous maintenance dose was a PP3M or

PP1M is immaterial. The point of using PP1M as a loading dose is to get the patient's drug concentration back to a steady state as quickly as possible. FOF ¶ 369. And the prior art taught that that could be done with two PP1M doses, one week apart. FOF ¶¶ 349, 351, 353. Moreover, general pharmacokinetic knowledge teaches using a faster-acting injectable for loading doses. FOF ¶¶ 151, 171. As such, a POSA would expect that a PP1M formulation would be faster-acting than a PP3M formulation due to its smaller particle sizes. *Id*.

Using PP3M without stabilizing with four or more months of PP1M: Janssen spent little time on this purported deficiency in the prior art. That too is not surprising. The JAMA prior art taught that for, initiating a patient, one would be stabilized with four or more months of PP1M. FOF ¶ 365. But a POSA certainly would not treat a patient that has drug in his or her body already in the same way. FOF ¶ 384. Instead, a POSA would know from the PP1M Prior Art that, in such a situation, two successive reinitiation loading doses of PP1M, one week apart, would return a patient to steady state. FOF ¶¶ 349, 351, 353. So treating a patient as naïve after four or more months of PP1M administration would not make sense to, or be advanced by, a POSA. FOF ¶ 161. Further, courts do not look to prior art in the "narrow, rigid" manner Janssen seeks to forward here. *KSR*, 550 U.S. at 420. "It is common sense that familiar items may have obvious uses beyond their primary purposes" and the initiation regimen for PP3M taught by JAMA—which uses PP1M to stabilize patients for a period of four months prior to their maintenance

doses of PP3M—is sufficient in combination with the PP1M missed-dose regimens to guide a POSA to the Asserted Claims. *Id.*

C. The Dependent Asserted Claims Were Taught by the Prior Art.

Aside from the missed-dose regimen of Claim 5, the other Asserted Claims, which all depend from Claim 5, are likewise disclosed by the prior art. Dr. Sommi did not offer any evidence that any of these dependent claims were valid or respond to Dr. Forrest's opinions as to those claims. FOF ¶ 424. As such, Mylan's evidence of obviousness regarding the other claims stands unrebutted.

That makes sense since each element of the dependent claims existed in the prior art. As stated *supra*, the prior art taught that PP1M and PP3M were effective for treating schizophrenia. FOF ¶ 418; *see also*, *id.* ¶¶ 182, 184. And psychosis is a "bucket term" that includes schizophrenia, so patients with schizophrenia are in need of treatment for psychosis as well. FOF ¶¶ 103, 417. Therefore, Claims 6 and 7 are taught by the prior art and obvious.

The PP1M Prior Art all taught a seven-day or one-week interval between the two PP1M loading doses in a reinitiation regimen. FOF ¶ 420. And the prior art, particularly the '519 Publication and Sustenna Label, taught an interval of thirty days or about one month between the second loading dose and the maintenance dose. *Id*. at 423. Claims 10, 11 and 14 are, therefore, disclosed in the prior art and rendered obvious.

IV. JANSSEN'S PURPORTED SECONDARY CONSIDERATIONS CANNOT AVOID OBVIOUSNESS

Janssen hid the ball on secondary considerations at trial, which made response difficult. The lack of commercial success, one secondary consideration, was addressed by Mr. Stec (on behalf of Mylan) and Ms. Mulhern (on behalf of Janssen). But Janssen was less forthcoming regarding any other potential secondary considerations. Janssen relied on Dr. Kohler for testimony solely related to secondary considerations. At trial, Dr. Kohler was unaware of which secondary consideration he was testifying to. Instead, he vaguely referred to an alleged "real world experience benefit." FOF ¶ 444. Real-world experience is not a secondary consideration under the law. But Dr. Kohler's confusion makes sense given that he was not provided with the relevant legal standards for his opinion on secondary considerations. Tr. 897:3-18 (Kohler). For that reason alone, Dr. Kohler's opinions as to secondary considerations should garner little, if any, credibility.

Despite the scope of Dr. Kohler's testimony, Janssen indicated in the Pretrial Order that it intends to offer legal analysis on the secondary considerations of commercial success, copying, and long-felt need. D.I. 99 at 101-102. All forms of secondary considerations require a "nexus," *i.e.*, a showing that the purported secondary consideration stems directly from the claimed invention as opposed to non-claimed features of the invention or prior art. *Merck & Cie v. Gnosis S.P.A.*, 808 F.3d 829, 837 (Fed. Cir. 2015). Further, even where a secondary consideration

exists, a patent is still invalid for obviousness where there is a strong *prima facie* case. *Genentech, Inc.*, 55 F.4th at 1378. But Janssen's only expert that addressed this issue, Ms. Mulhern, failed to establish any nexus between "the patented invention" and any evidence she contended supported commercial success.

A. Janssen's Evidence of Commercial Success Fails Because it Lacks Sufficient Nexus to the "Claimed Invention"

A patentee must establish a nexus between "the patented invention" and whatever evidence the patentee contends supports its commercial success. *Stratoflex, Inc. v. Aeroquip Corp*., 713 F. 2d 1530, 1539 (Fed. Cir. 1983); *Wyers v. Master Lock Co*., 616 F. 3d 1231, 1246 (Fed. Cir. 2010). To establish a nexus, a patentee can rely on either the "presumption of nexus" or the "nexus-in-fact." *Campbell Soup Co. v. Gamon Plus, Inc*., 10 F.4th 1268, 1276-77 (Fed. Cir. 2021). However, the presumption of a nexus is only available where the patent covers the main commercial embodiment. Here, that is not the case.[19] The claims cover a specific missed dosing regimen, not the FDA-approved use to treat schizophrenia.

This leaves Janssen only with a nexus-in-fact argument. Nexus-in-fact requires a "showing that the objective indicia are the direct result of the unique characteristics of the claimed invention rather than a feature that was known in the prior art." *Campbell Soup*, 10 F.4th at 1277 (internal citations omitted). JAMA

[19] To resolve Mylan's Motion *in Limine* No. 2, Janssen "confirmed that Ms. Mulhern will not testify as to any presumption of nexus with respect to her commercial success analysis." D.I. 102.

taught the safe and effective treatment of schizophrenia with a PP3M. As Dr. Stec explicitly explained during trial, Ms. Mulhern's analysis did not show that any commercial success was "a direct result of the unique characteristics of the claimed invention" and she did not offer any testimony that "the commercial success was not due to a feature that was known in the prior art." Tr. 1128:1-8 (Stec).

Rather, Ms. Mulhern only opined that "the Asserted Claims of the '693 patent [] contribute to the marketplace success of Invega Trinza" but did not opine on the legally relevant question as to whether any success is a "direct result" of the claimed invention as opposed to other factors. Tr. 1096:18-20 (Mulhern). *In re Huang*, 100 F.3d 135, 140 (Fed. Cir. 1996); *Campbell Soup*, 10 F.4th at 1277. Any commercial success of Trinza® is based on factors other than the claimed invention.

Ms. Mulhern relied on Dr. Kohler in her nexus analysis. Tr. 1090:7-9 (Mulhern). Even after Dr. Kohler explained that the label of Trinza included multiple different dosing regimens—*only one of which* is the four-to-nine month regimen of the Asserted Claims (Tr. 938:20-939:20 (Kohler))—Ms. Mulhern "didn't analyze specifically the contribution of the different dosing regimens . . . ." Tr. 1107:2-3, 1106:6-14 (Mulhern). Ms. Mulhern's entire analysis was not predicated on the commercial success of the claimed invention, *but the commercial success of Trinza as a whole* (including non-patented aspects). FOF ¶¶ 71, 473, 475. As *Campbell* makes clear, the commercial success must be "linked" to a

"claim's unique characteristics" and cannot include aspects that are "not claimed." 10 F.4th at 1279.

Ms. Mulhern's simplistic approach of looking at all sales metrics of a product to show commercial success of *the claimed invention* has been repeatedly rejected by the Federal Circuit. *In re Huang*, 100 F.3d at 140; *In re DBC*, 545 F.3d 1373 1384 (Fed. Cir. 2008). And that makes sense. It would be improper and unfair to credit the commercial success of a product due to elements that are "not claimed." *Campbell*, 10 F.4th at 1279. While Ms. Mulhern testified that, since its launch, Trinza® has generated $2.5 billion in total revenue, she knew that 83 percent of all Trinza® patients returned before the four-month interval required by the Asserted Claims. Tr. 1105:6-13 (Mulhern); Tr. 1131:1-19 (Stec). Therefore, the "large majority" of the revenues and growth that Ms. Mulhern attributed to the claimed invention had nothing to do with the claims so could not be a "direct result" of the claimed features. Tr. 1131:14-19 (Stec), Tr. 1128:1-8 (Stec), Tr. 1127:3-5 (Stec); *see also Ormco Corp. v. Align Technology, Inc*., 463 F.3d 1299, 1313 (Fed. Cir. 2006) (no nexus when commercial success is due only "in part" to claimed features).

Ms. Mulhern's failure to properly analyze nexus-in-fact does not end there. In *Campbell*, the Federal Circuit explained that this inquiry also accounts for any alleged commercial success resulting from what "was known in the prior art." 10 F.4th at 1277. As explained above, JAMA disclosed using paliperidone palmitate

in three-month intervals. Ms. Mulhern did not separate out any contribution of using paliperidone palmitate in three-month intervals in her analysis, which would constitute the vast majority of Trinza® prescriptions. Tr. 1038:23-1039:1 (Berger), Tr. 1039:11-15 (Berger); Tr. 1131:14-19 (Stec), Tr. 1128:1-8 (Stec), Tr. 1127:3-5 (Stec). Failing to account for what "was known in the prior art" is yet another reason Janssen has failed the nexus-in-fact inquiry. *Campbell*, 10 F. 4th at 1278 (no nexus where the patentee "presented evidence that merely ties commercial success and praise to aspects . . . that were already present in the prior art").

Put simply, all Janssen has shown is that Trinza® *as a whole* has certain financial metrics; Janssen presented no "proof that the sales were a direct result of the unique characteristics of the **claimed invention**—as opposed to other economic and commercial factors unrelated to the quality of the patented subject matter." *Huang*, 100 F.3d at 140. Further, Janssen has not accounted for the prior art's teachings in its analysis. Having not done so, Janssen has not shown a nexus-in-fact and, therefore, secondary considerations cannot rebut the strong *prima facie* obviousness case. *Campbell*, 10 F.4th at 1277.

B. Janssen Did Not Establish Industry Praise

Evidence of praise "by others" or the "industry" generally that is "specifically related to the features of the patented invention" can be a secondary consideration. *Power-One, Inc. v. Artesyn Technologies, Inc.*, 599 F. 3d 1343, 1352 (Fed. Cir. 2010). That praise, however, should be from a competitor or "by others."

Power-One, 599 F.3d at 1352 (citing *Allen Archery, Inc. v. Browning Mfg. Co*., 819 F.2d 1087, 1092 (Fed. Cir. 1987) (praise in the industry and specifically praise from a competitor, tends to "indicat[e] that the invention was not obvious")).

Here, the only evidence of alleged industry praise is from Janssen-affiliated materials. Tr. 882:6-12, 913:20-915:8 (Kohler). Evidence affiliated with the patentee "fall[s] well short of demonstrating true industry praise" since it is not praise by the "industry" or "others." *Bayer Healthcare Pharm. Inc. v. Watson Pharm. Inc*., 713 F.3d 1369, 1377 (Fed. Cir. 2013). But what diminishes Janssen's purported evidence even further is that the alleged praise does not even constitute praise within the meaning of the law. As Dr. Kohler testified, those proffered Janssen articles only "identif[y]" or "mention" the existence of the claimed dosing regimen. Tr. 882:6-12 (Kohler), Tr. 913:20-915:8 (Kohler). Nowhere is there "praise" of the missed-dosing information required by the claims.

C. The Asserted Claims Did Not Satisfy a Long-Felt but Unmet Need

Evidence of long-felt but unmet need that existed as of the patent's filing date and was satisfied by an invention may be evidence of secondary considerations of nonobviousness. *Perfect Web Techs., Inc. v. InfoUSA, Inc*., 587 F.3d 1324, 1332 (Fed. Cir. 2009). As Dr. Berger testified the long felt but unmet need is adherence (*i.e.*, ensuring patients stay on their medication). Tr. 1039:11-25 (Berger). Both experts agreed that patients still miss their doses of Trinza® despite the claimed missed-dose information; the claimed invention does nothing to prevent patients

from missing doses. Tr. 873:25-874:2 (Kohler); Tr. 872:3-5 (Kohler); Tr. 1035:14-20 (Berger), 1040:7-1041:12 (Berger).

Not only does the claimed missed-dose information fail to satisfy the long-felt need, but there is little evidence that such information is even used. Dr. Kohler testified (without any evidentiary support) that there are a very small number of patients that fall within the Asserted Claims' four-to-nine month window and, even for those patients, he has only used the claimed dosing regimen less than about half the time. Tr. 935:3-21 (Kohler), Tr. 888:19-21 (Kohler). Dr. Berger testified that he has never followed the claimed dosing regimen for Trinza®, administering PP3M instead of the claimed PP1M reinitiation doses. Tr. 231:1-8 (Berger); Tr. 262:3-7 (Berger); Tr. 1043:20-24 (Berger). Like Dr. Berger, even Janssen's own Joshi paper (FOF ¶ 7, fn. 2 (DTX-176)) that tracked patients taking PP1M and PP3M failed to show a single patient that followed the claimed reinitiation dosing regimen; all data showed administration of only PP3M in the claimed missed-dosing window. Tr. 1112:3-6 (Mulhern), Tr. 1113:25-1114:7 (Mulhern); Tr. 1130:22-25 (Stec), Tr. 1155:10-25 (Stec), Tr. 1156:4-21 (Stec), Tr. 1180:9-17 (Stec). As such, the claims can hardly be said to have "satisfied" any long-felt but unmet need that Janssen attempted to portray. *Perfect Web*, 587 F. 3d at 1332.

D. Janssen Did Not Establish a Showing of Unexpected Results of the Claimed Invention

"[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art." *Kao Corp. v. Unilever United States, Inc.*, 441 F.3d 963, 970 (Fed. Cir. 2006) (emphasis added). As explained during trial, JAMA taught the paliperidone palmitate three-month formulation and its use. *See generally* DTX-026; Tr. 445:6-12 (Forrest). Consistent with JAMA, Dr. Berger testified that, when faced with a patient who returns in the claimed four-to-nine month dosing window, he administers a dose of PP3M rather than the claimed dosing regimen. Tr. 231:1-8 (Berger); Tr. 262:3-7 (Berger); Tr. 1043:20-24 (Berger). Joshi does the same. Tr. 1112:3-6 (Mulhern), Tr. 1113:25-1114:7 (Mulhern); Tr. 1130:22-25 (Stec), Tr. 1155:10-25 (Stec), Tr. 1156:4-21 (Stec), Tr. 1180:9-17 (Stec). Therefore, medical professionals do in fact treat patients in the claimed dosing window with PP3M consistent with the prior art. Tr. 231:1-8 (Berger); Tr. 262:3-7 (Berger); Tr. 1043:20-24 (Berger). Whatever "real world experience benefit" Dr. Kohler believes the claimed invention provides, he and Janssen have failed to compare that alleged benefit with the closest prior art. Therefore, Janssen cannot show unexpected results to overcome Mylan's strong *prima facie* obviousness case. See Kao Corp., 441 F.3d at 970.

V. THE ASSERTED CLAIMS ARE INVALID UNDER 35 U.S.C. § 112

Both the inquiry for enablement and that for written description compare the scope of the claims to the disclosure of the specification. *Sitrick v. Dreamworks, LLC*, 516 F.3d 993, 1000 (Fed. Cir. 2008) ("An enablement analysis begins with

the disclosure in the specification"); *Union Oil Co. v. Atlantic Richfield Co*., 208 F.3d 989, 998 (Fed. Cir. 2000) (written description is based on the "patent's description"). As discussed *supra*, a POSA would know that different formulations would be likely to result in different pharmacokinetics, which is the reason Invega Sustenna® and Trinza® utilize almost identical ingredients. FOF ¶¶ 194, 493. Here, the Asserted Claims cover millions of different formulations made with a number of different ingredients. FOF ¶ 486. The vast majority of these were never created, much less tested, used in clinical trials, or modeled with popPK data. FOF ¶¶ 487, 490. The specification of the '693 patent merely discloses, at most, two nearly identical PP1M formulations—the F011 and F013 formulations—and a single PP3M formulation. FOF ¶ 490. Because of this vast discrepancy between the narrow scope of disclosure in the specification (a small number of formulations) and scope of claims (millions), the Asserted Claims are invalid.

A. Claims Are Invalid For Lack Of Enablement

Under 35 U.S.C. § 112, a patent must disclose sufficient information to enable others to practice the "full scope of the claimed invention." *Sitrick v. Dreamworks,* 516 F.3d at 999; *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003) ("The requirement of enablement… enforces the essential '*quid pro quo* of the patent bargain' by requiring a patentee to teach the public how 'to practice the full scope of the claimed invention.'"). Enablement is an "prevents both inadequate disclosure of an invention and overbroad claiming that might otherwise

attempt to cover more than was actually invented. Thus, a patentee chooses broad claim language at the peril of losing any claim that cannot be enabled across its full scope of coverage." *MagSil Corp. v. Hitachi Global Storage Technologies*, 687 F.3d 1377, 1381-82 (Fed. Cir. 2012).

"A patentee who chooses broad claim language must make sure the broad claims are fully enabled. The scope of the claims must be less than or equal to the scope of the enablement to ensure that the public knowledge is enriched by the patent specification to a degree at least commensurate with the scope of the claims." *Sitrick*, 516 F.3d at 999 (quotations and citations omitted). Here, too, if Janssen wants to "exclude others from what it regard[s] is its invention, its patent need[s] to teach the public how to make and use that invention." *Trustees of Bos. Univ. v. Everlight Elecs. Co.*, 896 F.3d 1357, 1365 (Fed. Cir. 2018). Janssen and its patent failed to do so.

Although "a specification need not disclose what is well known in the art," "[t]ossing out the mere germ of an idea does not constitute enabling disclosure." *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997). "To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997). In order to assess whether a claim requires undue experimentation, courts rely on the *Wands* factors. *See, e.g.*, *Pac. Biosciences of*

California, Inc. v. Oxford Nanopore Techs., Inc., 996 F.3d 1342, 1350 (Fed. Cir. 2021). These factors include: "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988). However, a court does not need to assess each factor in every case to make its determination. *Id*.

1. The Asserted Claims Are Broad and the Nature of the Invention Cuts Against Enablement

The Asserted Claims of the '693 patent are not limited to a single (or specific) PP1M or PP3M formulation; instead, they claim generally PP1M and PP3M formulation(s). FOF ¶¶ 481-82. As if that were not broad enough, they use the claim term "comprising," meaning cited elements are only a part of the claimed formulations and, thus, the claim can encompass additional, unrecited elements. *MagSil*, 687 F.3d at 1383. And these formulations must be suitable to reinitiate a PP3M patient back to steady state plasma levels, according to the administration steps in the claim. But turning to the specification in order to determine the bounds of "a" PP1M formulation and "a" PP3M formulation provides no metes and bounds that could inform the public as to where such formulations begin or end. FOF ¶¶ 483-86. The specification provides wide ranges of excipients and corresponding

concentrations, resulting in thousands, if not millions, of permutations all of which would be included within the claims. *Id*. Further, as explained above, particle size and structural elements impact the pharmacokinetics of a formulation, yet the claims do not recite *any* limitations on such structural elements. FOF ¶¶ 483, 494. This would mean that claims include particle sizes to which the specification provides, at best, broad potential ranges. For example, ranges for the PP1M formulations vary from 2000 to 100 nanometers. FOF ¶¶ 485, 489. That is a twenty-fold difference from one end of the disclosed range to the other. *Id*. The PP3M range is similarly broad, covering 20 to 3 microns, or a six-fold difference. *Id*. As Dr. Forrest testified, just the ranges of particle sizes and excipients within the '693 patent could lead to over ten million possible combinations. FOF ¶ 486. In fact, Janssen told the examiner during prosecution of the '693 patent that the different nanoparticle sizes of PP1M and PP3M make these "vastly different" formulations and affect the way PP1M and PP3M perform in the body. FOF ¶ 488. Mylan's and Janssen's experts agree that changing particle size, injection volume, and excipients all can change the pharmacokinetics of a formulation. FOF ¶¶ 493-94. After any such change, a POSA would then need to test each combination to ensure its viability with the specific claimed dosing regimen. FOF ¶ 493.

In *Wyeth and Cordis Corp. v. Abbott Labs.*, the Federal Circuit held a patent invalid for lack of enablement because the full scope of the claims required a POSA to "synthesize and screen each of at least tens of thousands" of compounds. 720

F.3d 1380, 1385 (Fed. Cir. 2013). The Court found this amount of testing constituted undue experimentation. *Id.* Although "a considerable amount of experimentation is permissible" under *Wands*, this proposition is "not without bounds." *Id.* at 1386 (citing *Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 1360-61 (Fed. Cir. 1998) (internal quotation omitted); *Cephalon, Inc. v. Watson Pharm., Inc.*, 707 F.3d 1330, 1339 (Fed. Cir. 2013)). As in *Abbott Labs.*, the '693 patent specification discloses only, at best, a "starting point" for further research. *Id.* at 1386. Further, the '693 patent would require testing of over ten million compounds rather than the tens of thousands the Federal Circuit found to be excessive in *Abbott Labs*. The full scope of the asserted claims is not enabled.

2. Lack of Guidance in the Specification and Absence of Working Examples Cut Against Enablement

Courts have evaluated the *Wands* factors for lack of guidance in the specification and the presence or absence of working examples together. *See, e.g., Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149, 1160 (Fed. Cir. 2019). Lack of guidance in the specification and presence or absence of working examples are found insufficient when they are not "commensurate in scope with the claim." *In re Hyatt*, 708 F.2d 712, 714 (Fed. Cir. 1983). Identification of categories is not enough; a patentee must also disclose which items in a category "effectively treat" the targeted issue. *Idenix*, 941 F.3d at 1160.

Here, Janssen was required to do more than list broad categories of excipients and broad ranges of particle sizes. It was required to identify which excipients and particle sizes would work in the manner set forth by the claims, *i.e.*, to reinitiate patients safely and effectively on PP3M after they have missed a scheduled dose. This requires identifying formulations commensurate with the scope of the claims that would bring patient plasma levels back to steady state. Reliance on a POSA to fill in any gaps in the specification cannot paper over a patentee's failure to enable practice of the asserted claims. "A specification that requires a POSA to 'engage in an iterative, trial-and-error process to practice the claimed invention' does not provide an enabling disclosure." *Idenix*, 941 F.3d at 1161 (quoting *ALZA Corp. v. Andrx Pharm., LLC*, 603 F.3d 935, 941 (Fed. Cir. 2010)). In other words, Janssen had an obligation to adequately disclose and enable its invention in the specification and the knowledge of a POSA cannot "serve as a substitute for the missing information in the specification." *ALZA Corp*., 603 F.3d at 941.

B. The Asserted Claims Lack Sufficient Written Description and Are Therefore Invalid.

The specification of the '693 patent does not disclose enough information to establish possession of the invention. *University of Rochester v. GD Searle & Co*., *Inc.,* 358 F.3d 916, 920 (Fed. Cir. 2004) ("The purpose of the written description requirement is to "ensure that the scope of the right to exclude, as set forth in the

claims, does not over-reach the scope of the inventor's contribution to the field of art as described in the patent specification").

The specification of the '693 patent merely discloses, at most, two nearly identical PP1M and PP3M formulations that are suitable to be used in the claimed dosing regimen, *i.e.*, the F011 and F013 formulations. FOF ¶ 490. The claims, however, cover far more than these two disclosed formulations, in no way being limited to the two PP1M and PP3M formulations. Rather, the claims cover *any* PP1M and PP3M formulation. Put another way, Janssen claimed "a" formulation of both PP1M and PP3M, using general and wide ranges of elements of such formulations in the specification. FOF ¶¶ 481-82. Janssen did so in order to ensnare *any* PP1M and PP3M formulation whether submitted to the FDA pursuant to the Hatch-Waxman Act or under any of the other provisions. Allowing Janssen to claim such a broad range of formulations without it "perform[ing] the difficult work of producing a complete and final invention featuring all of its claimed limitations and publicly disclos[ing] the fruits of that effort" is an affront to the *quid pro quo* of the patent system. *Biogen Int'l GMBH v. Mylan Pharms. Inc*, 18 F.4th 1333, 1344 (Fed. Cir. 2021). Other than the two formulations described in the specification, Janssen did not have possession of the recited PP1M or PP3M formulations that fall within the scope of the claims. Put simply, the specification does not "describe the invention sufficiently to convey to a person of skill in the art that the patentee had possession of the claimed invention at the time of the

application, i.e., that the patentee invented what is claimed." *LizardTech, Inc. v. Earth Resource Mapping, Inc*., 424 F. 3d 1336, 1345 (Fed. Cir. 2005).

That the '693 patent does not disclose enough information to establish possession of the claimed invention beyond only two embodiments, is further evidenced by the fact that, during prosecution, Janssen told the examiner that the different nanoparticle sizes of PP1M and PP3M make these "vastly different" formulations and affect the way PP1M and PP3M perform in the body. FOF ¶ 488. At trial, Janssen's expert confirmed that other facets of the formulation impact the pharmacokinetics in unpredictable ways. FOF ¶ 494. Given the limited disclosure of the specification, a POSA would not conclude that the inventors had possession of any PP1M or PP3M formulation. *Cf. LizardTech*, 424 F.3d at 1346.

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